Cyclic fatigue resistance of nickel titanium rotary files in the martensitic state: a systematic review.

By

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Abbreviations and symbols

NiTi	Nickel Titanium
SIM	Stress Induced Martensite
A_s	Austenite start temperature
A_f	Austenite finish temperature
M_s	Martensite start temperature
M_f	Martensite finish temperature
R_s	R-phase start temperature
R_f	R-phase finish temperature
CM	Controlled memory
DSC	Differential scanning calorimetry
™	Trade Mark
rpm	Rotations per minute
Ncm	Newton centimetre
mm	Millimetre
F1	Finishing File size 25
F3	Finishing file size 30
NaOCl	Sodium hypochlorite
HEBP	Etidronic acid
EDTA	Ethylene diamine tetra acetic acid
°C	Degrees Celsius
°	Degree or angle measured in degrees
NCF	Number of cycles to fracture
ML	Mean life in seconds
TTF	Time to fracture in seconds
SEM	Scanning electron microscope

Abstract

Background

There are many factors which effect the cyclic fatigue resistance of Nickel titanium or NiTi files. The metal can exist in a soft martensitic state which is thought to improve the resistance to cyclic fatigue. The NiTi alloy transforms from one state to the other at a certain temperature and various factors can modify this transition temperature. Temperature effects the state of the metal so the way the file acts at intracanal temperature is significant. Most cyclic fatigue tests have been carried out at room temperature.

Objectives

Identifying martensitic files and whether the resistance to cyclic fatigue is greater in these files at intracanal temperature.

Methods

A PICOS is used to formulate the review question. It provides a framework to develop inclusion and exclusion criteria. Search terms are used on the databases Science Direct, Wiley, PubMed and Google Scholar. A single reviewer screened the results, applying inclusion and exclusion criteria. The results are analysed and a descriptive analysis carried out. A Joanna Briggs checklist for cohort studies is used to assess the quality of the studies. An assessment of bias in the primary studies and bias in the review process is carried out.

Keywords: cyclic fatigue, martensitic, intracanal temperature, CM files, Gold files, Blue files, EDM files.

Results

The overall quality of the included studies was judged as moderate. However, cyclic fatigue testing methods have no standardisation, so it is difficult to compare studies. Many studies did not show evidence of sample size calculation and this was not taken into consideration by the scoring system for quality assessment. Within the limitations of the study it is found that at intracanal temperature, Hyflex EDM™ is potentially martensitic, existing in the R-

phase which is considered to be a martensitic phase. It is also found that a wide range of 30.8 °C – 36 °C exists for intracanal temperature.

Conclusions

Within the limitations of the study it is found that the Hyflex EDM file is martensitic at intracanal temperature and has a higher cyclic fatigue resistance than the other martensitic phase files. Most of the martensitic phase files identified possessed a greater cyclic fatigue resistance than the other files tested.

Declaration

I declare that this thesis is my original work and has not been submitted previously for any award or course.

Trisalda Harrison

September 2019.

Acknowledgements

I would like to thank my supervisor, Steve Cowling for his support and guidance. I would also like to thank Mike Horrocks, David Baker and the rest of the Simply-Endo team for all their support.

Introduction

The presence of bacteria within the root canal space is the most common cause of endodontic pathology (Kakehashi, Stanley & Fitzgerald, 1965; Ørstavik & Pitt Ford, 2007). The treatment of endodontic disease involves the use of instruments to widen the canal and allow disinfection of the canal space (Segura-Egea, Martin-Gonzalez & Castellanos-Cosano, 2015). Files are instruments which are used to widen canals and can be made of stainless steel or nickel titanium alloy. Nickel Titanium or NiTi alloy was developed by the Naval Ordinance Laboratory, it is called Nitinol which stands for Nickel, Titanium and “nol” stands for the laboratory initials (Zupanc, Vahdat-Pajouh & Schäfer, 2018). The flexibility of NiTi has allowed the files to be used in rotary motion in a handpiece, which has enabled preparation of the canal space to be less time consuming and more efficient. NiTi files are some of the instruments used to widen the canal but if a file separates or fractures, this can prevent the complete cleaning of the canal space (Nevares, Cunha, Zuolo & Da Silveira Bueno, 2012; Terauchi, 2016).

Terauchi (2016) claims the incidence of file fracture or separation to be in a wide range of 0.4% to 23%. If the separated instrument cannot be retrieved and apical pathology persists; surgical treatment or extraction may be necessary. The patient must be informed of the risk of file fracture before the treatment starts, when it happens and then options and risks associated with retrieval or retention of the broken fragment before removal is attempted (McGuigan, Louca, & Duncan, 2013; Terauchi, 2016). The process to remove a separated file is time consuming and expensive to either the patient or the dentist, depending on who decides to bear this cost (Machtou, 2010; Kaval, Capar & Ertas, 2016). The procedure can remove tooth structure and this can lead to over preparation of the canal space, which could weaken the remaining tooth structure resulting in fracture of the tooth or vertical root fracture (Bier, Shemesh, Tanomaru-Filho, Wesselink, & Wu, 2009; Machtou, 2010). The presence of a fragment of separated instrument in the canal does not affect the outcome but it is the presence of bacteria and the inability to clean the canal completely beyond the retained fragment that may lead to a poor prognosis (Panitvisai, Parunnit, Sathorn & Messer, 2010; Terauchi, 2016). If the separated instrument cannot be removed, it may be possible to bypass it, to clean the remaining portion of the canal beyond the separated instrument but there is a risk that the procedure could cause a perforation or a ledge especially if the canal is curved (Nevares et al., 2012). These iatrogenic errors can complicate treatment, so the prevention of instrument separation is beneficial for both the clinician and the patient (McGuigan et al., 2013; Terauchi, 2016).

1.1. What causes instrument separation?

Fatigue or weakening of the metal results in instrument separation, it can be cyclic or torsional (Anderson, Price & Parashos, 2007; Pedulla et al., 2016; Arias, De Vasconcelos, Hernández & Peters, 2017). Torsional fatigue occurs when the tip of the file is locked inside the canal whilst the main body or shaft of the file continues to rotate, which results in the metal reaching its elastic limit rapidly and the instrument separating suddenly. The elastic limit is defined as the maximum ability of a metal to be stretched without permanent change or deformation (Campbell, Shen, Zhou & Haapasalo, 2014; Terauchi, 2016). The signs of torsional fatigue can often be visible as the instrument unwinds or elongates; so careful inspection of the instrument during use and replacement when signs of deformation are visible, can help prevent fracture by torsion (Wycoff & Berzins, 2012; Al-Hadlaq, 2013).

Cyclic fatigue occurs as the file rotates in a curved canal and is being subjected to tensile and compressive strains as it rotates (Wycoff & Berzins, 2012; Ferriera et al., 2017). Tension is being stretched, whilst compression pushes the material together. During each rotation of the file around a curvature, the strain or force can cause compression of half of the file facing the inner curve, whilst tension occurs on the half of the file facing the outer curve (Figure 1.1). Then when the file rotates, the portion that was subjected to tension is now compressed and the compressed half is subjected to tension. This occurs repeatedly with each cycle of rotation, resulting in crack initiation on the metal surface, which leads to the propagation of the crack, eventually resulting in instrument separation (Pedulla et al., 2015; Terauchi, 2016). Unfortunately, cyclic fatigue does not give the clinician visible signs of the instrument deforming which makes it difficult to prevent in practice (Anderson et al., 2007; Carvalho, Freitas, Reis, Montalvao & Fonte, 2015).

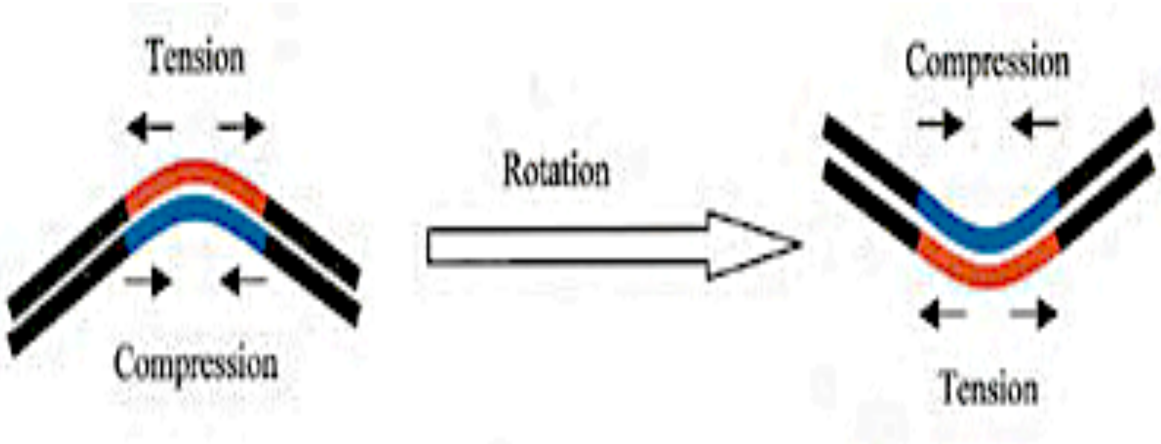


Figure 1.1. Cyclic fatigue occurs as stresses on the file change during each rotation. From “Rotary nickel titanium instrumentation” by Dr. Mounce, 2004, Dentistry Today, (http://www.dentistrytoday.com/endodontics/1085-rotary-nickel-titanium-instrumentation).

Although, each type of fatigue is studied separately, it can occur simultaneously within a canal, especially in a narrow and curved canal. Torsional resistance is decreased in instruments that have been stressed by cyclic fatigue; whilst instruments stressed by high torque show a lower resistance to cyclic fatigue (Campbell et al., 2014; Terauchi, 2016; Pedulla et al., 2016).

1.2. What is the martensitic state in nickel titanium?

Zupanc et al. (2018) states that the nickel titanium alloy which is used to make endodontic files has 56% nickel and 43% titanium by weight, or an atomic ratio of 1 to 1, with NiTi alloy having three states or phases which are the austenitic state, r-phase and the martensitic state. The austenitic state is rigid and will spring-back to its original shape after being bent; whilst the martensitic phase is more flexible, can hold its shape when bent and does not spring back to its original shape. The austenitic instruments have an elastic limit of

7% which means after being stretched to this limit it deforms, whilst martensitic instruments show signs of deformation sooner and unwind (Terauchi, 2016). The R-phase is a phase between these two phases and is considered a phase towards the martensitic phase or a variant of the martensitic phase (Aoun, Nehme, Naaman, & Khalil, 2017; Zupanc et al., 2018). The nickel titanium alloy can be transformed from one stage to the next by a change of temperature or the application of stress but it is the state that it is in at the intracanal temperature, which differs from room temperature, that is important to the clinician. This is dependent on the processes that the alloy undergoes during the production of the file, such as heat treatments and cold working, which can result in the metal being predominantly in one phase or a mixture of phases (Terauchi, 2016; Zupanc et al., 2018). Files which have more of the martensitic phases are more flexible and have increased cyclic fatigue resistance, which can help prevent instrument separation in curved canals (Campbell et al., 2014; Terauchi, 2016).

1.3. Why is it important to do a systematic review of cyclic fatigue of martensitic files?

A systemic review can provide evidence for clinicians to follow and can give guidance on a particular issue (Drucker, Fleming & Chan, 2016; Baird, 2018). The literature is reviewed in a systematic way which is reproducible and reduces the possibility of errors and bias (Higgins & Green, 2011; Baird, 2018; Linares-Espinós et al., 2018). There are currently a lot of claims by manufacturers regarding the cyclic fatigue resistance of martensitic files but a systematic review of the literature has not been carried out. Pirani et al. (2016) claim that Hyflex EDM files have a cyclic fatigue resistance of 700% when compared to Hyflex CM™ files and this has been used by manufacturers Coltene, in their catalogue, to promote the file. However, a closer look at this study reveals that this claim for the 700% increase in fatigue resistance is for a size 40 Hyflex EDM file; whilst the size 25 file, which is the most commonly used size, has a 41% increase in its cyclic fatigue resistance compared to the corresponding size in the Hyflex CM file. Both Pirani et al.(2016)

and the manufacturer concentrated on the 700% figure rather than 41%, as it seemed more convincing.

There are many files available on the market, with each differing in taper, design and characteristics of the metal, for example, Vortex Blue™, ProTaper Gold™ and Hyflex EDM. It is better to prevent file separation and this requires knowledge of when to use a particular type of file as the various characteristics of the file have an influence on separation (Campbell et al., 2014; Terauchi, 2016). A systematic review can help identify gaps in the literature and can highlight areas for future research (Higgins & Green, 2011; Siddaway, 2014). Therefore, a systematic review of the literature with an aim to understand the evidence available on how the martensitic state effects cyclic fatigue resistance of NiTi files is carried out.

1.4. Aims and Objectives

The aims and objectives are:

- Identify the types of martensitic phase files available.
- Review the factors affecting the cyclic fatigue resistance in martensitic files.
- Identify and include any studies on cyclic fatigue resistance in martensitic phase files.
- Evaluate the included studies and provide a descriptive analysis (Higgins & Green, 2011).
- Highlight gaps in the literature and areas for future research (Higgins & Green, 2011).

Background

A review of the literature available using searches on the Science direct database revealed factors which effect the cyclic fatigue resistance in NiTi files.

2.1. Factors which effect cyclic fatigue resistance

- The curvature of the root canal and the type of tooth (Young, Parashos & Messer, 2007; Ahn, Kim & Kim, 2016; Terauchi, 2016).
- The instrument design which can be size, shape, alterations in cross section and taper of the file (Ahn et al., 2016; Gündoğar & Özyürek, 2017).
- The surface treatment of the file (Campbell et al., 2014; Gündoğar & Özyürek, 2017).
- The torque applied to the instrument (Young et al., 2007; Ahn et al., 2016; Terauchi, 2016).
- The movement or kinematics of the file, which can be either continuous rotary or reciprocation (Ahn et al., 2016; Gündoğar & Özyürek, 2017).
- The instrumentation technique, for example, single versus multiple file systems and the use of a glide path (Campbell et al., 2014; Terauchi, 2016).
- The speed of rotation of the file (Ahn et al., 2016; Terauchi, 2016).
- The level of skill of the operator (Young et al., 2007; Campbell et al., 2014; Terauchi, 2016).
- The presence of irrigants and debris in the canal (Bennett, Chung, Fong, Johnson & Paranjpe, 2017).
- The type of alloy (Ahn et al., 2016; Gündoğar & Özyürek, 2017).
- The process to manufacture the file (Ahn et al., 2016; Gündoğar & Özyürek, 2017).
- The intracanal temperature or temperature within the canal when the instrument is in use (Grande et al., 2017; Zupanc et al., 2018).

2.1.1. The curvature of the canal and type of tooth

Fracture of a NiTi rotary file due to cyclic fatigue, commonly occurs in the curved portion of the root canal (Wycoff & Berzins, 2012; Alshwaimi, 2017). Ansari and Maria (2012) stated that the root canal can curve in different areas of the root, such as the middle third or apical third of the root and that these curvatures can be gradual or abrupt. A radiograph is usually taken of the tooth prior to treatment to assess pathology and visualise root anatomy (Figure 2.1) but the canal can have a double curve, or the curve could be s-shaped in the buccolingual plane, which cannot be easily visualised on a radiograph as it is in a mesiodistal plane (Figure 2.2).

Figure 2.1. Radiograph showing the severe root curvature of lower mandibular second premolar. From “Managing curved canals,” by I. Ansari & R. Maria, 2012, *Contemporary Clinical Dentistry*, *3*(2), p. 237.

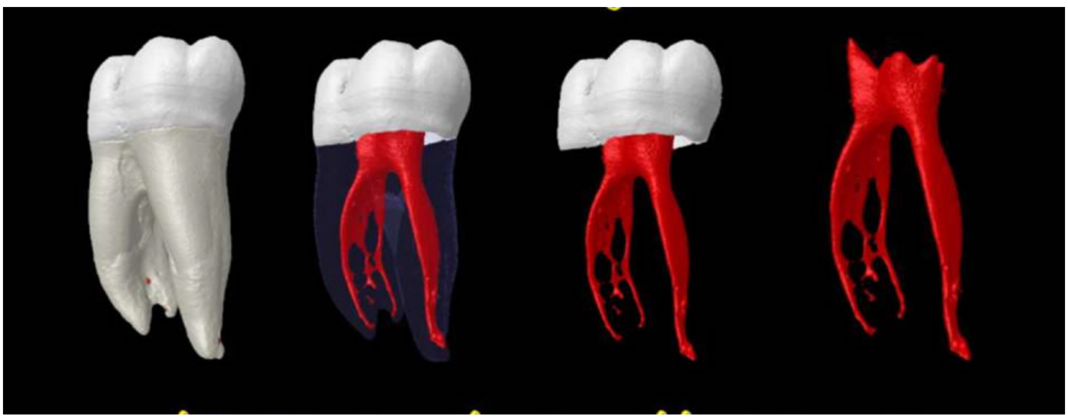


Figure 2.2. Diagram of root canal space (red) showing the complexities of root canal anatomy like canals merging and curving in three dimensions which may not be visible on a two-dimensional radiograph. From “Root canal anatomy is complex,” by P.Q. Shelley, 2012, (http://www.elmendo.com/2012/02/root-canal-anatomy-is-complex/).

The canal can branch into a network or an apical delta or have connections with adjacent canals in the form of isthmuses (Vertucci, 2005; Gutmann & Fan, 2016). When an abrupt curvature occurs in the apical third of the root, any separated instrument in this region is more difficult to retrieve as visualisation is difficult, with the risk of damage or perforation of the root; visualisation of the separated instrument doubles the success of removing it (Nevares et al., 2012; McGuigan et al., 2013). A lower success in removal is found to be when the degree of the root canal curvature is in the range of 21° to 50° (Cuje, Bargholz & Hülsmann, 2010). The NiTi files, which can be 21 – 31 mm long, are fixed to a hand piece which rotates the file but adds another 10 mm to the length; as a result when working on a posterior tooth, like a second molar, this can mean that the file is bent before being subjected to bends within a curved canal. Patel and Rhodes (2007) and Gutmann and Fan (2016) have explained that straight-line access into a root canal is created when ledges and obstructions are removed to allow an instrument to be placed vertically into the canal (Figure 2.3).

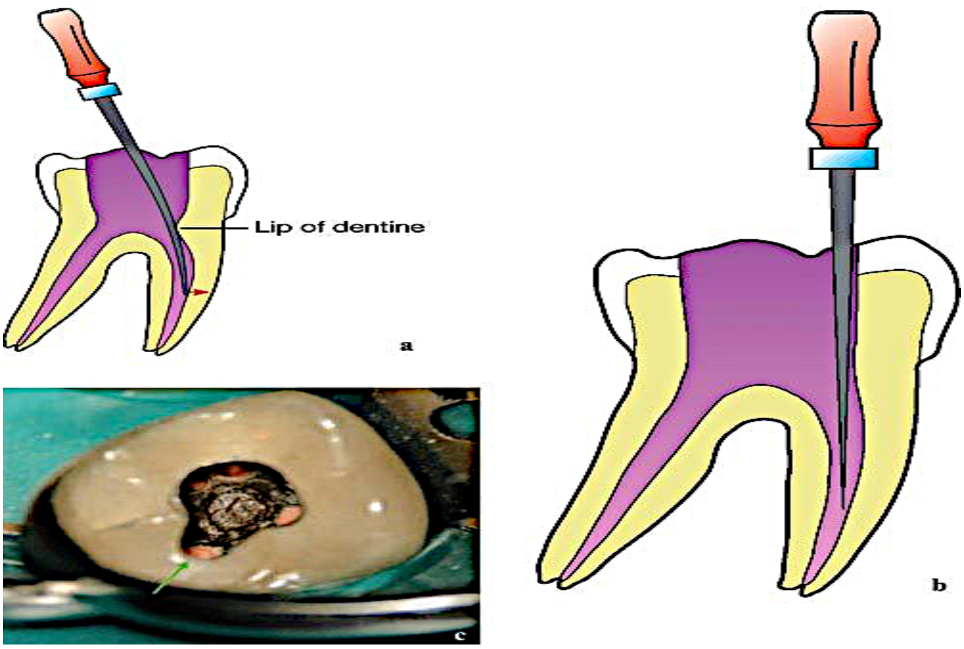


Figure 2.3. Straight-line access (a) Inadequate straight-line access resulting in the tip of the file attempting to straighten itself (red arrow). (b) Removing the lip of dentine results in straight-line access into the root canal. (c) The mesiobuccal corner of the access cavity has been extended (green arrow) to give straight-line access into the mesiobuccal canal of this crowned lower tooth. From ”A practical guide to endodontic access cavity preparation in molar teeth,” by S. Patel and J. Rhodes, 2007, *British Dental Journal*, *203*(3), p. 136.

Whilst straight-line access to the canal is preferred, in some cases this may not be possible without removing a lot of tooth structure, especially when access is limited, so there will be a higher risk of instrument separation (Figure 2.4). Instrument separation seems to occur more in mandibular molars which may be due to access and the complex anatomy of the canals (Cuje et al., 2010; Nevares et al., 2012; Terauchi, 2016). The martensitic files have shape memory, allowing them to be pre-curved to hold their shape, which is an advantage in situations where access is difficult (Zupanc et al., 2018); more conventional files like austenitic files do not have this ability (Figure 2.5).

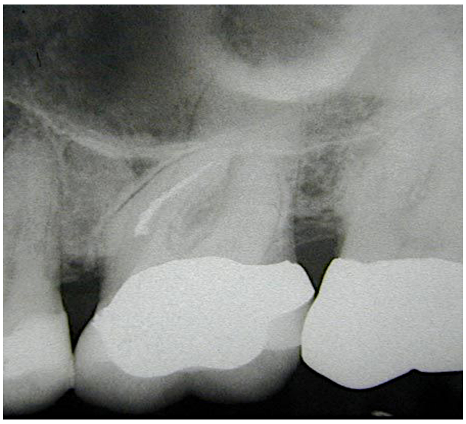


Figure 2.4. Radiograph showing a crowned molar tooth with a separated NiTi instrument in a very curved root where inadequate straight-line access could have been a factor. From ”A practical guide to endodontic access cavity preparation in molar teeth,” by S. Patel and J. Rhodes, 2007, *British Dental Journal*, *203*(3), p.137.

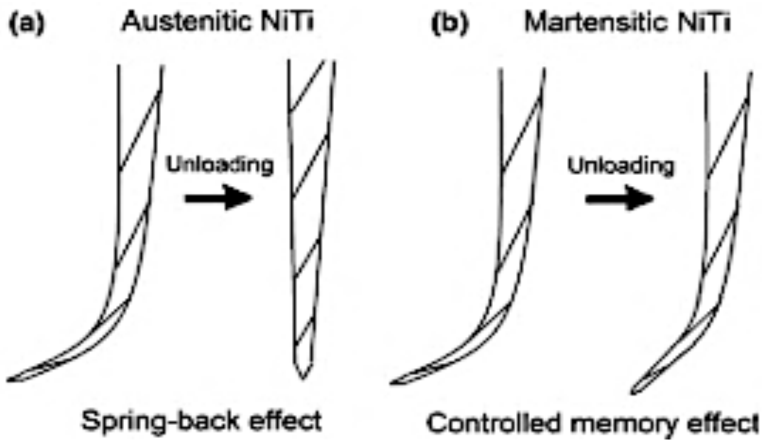


Figure 2.5. The Martensitic file can be pre-curved and maintains the new shape but the austenitic file springs back when the force or load is removed. From “New thermomechanically treated NiTi alloys - a review,” by Zupanc et al., 2018, *International Endodontic Journal*, 5(10), p. 1094.

2.1.2. The instrument design

NiTi rotary files come in different sizes, with larger sized instruments being stiffer than those which are smaller (Young et al., 2007). Sanghvi and Mistry (2011), and Khasnis, Kar, Kamal and Patil (2018) mention that in curved canals, stiffer files can be subjected to cyclic fatigue and break more easily than files which are more flexible. The instrument tip size can be small but moving up the shaft of the instrument, it gets wider and how quickly it gets wider can vary. This is called the taper of the instrument and it is possible for the same instrument to have different tapers in different sections (Figure 2.6). The design of the instrument cross section can vary from circular, square, rhomboid or trapezoid and this can vary in different sections of the same file (Figure 2.7).

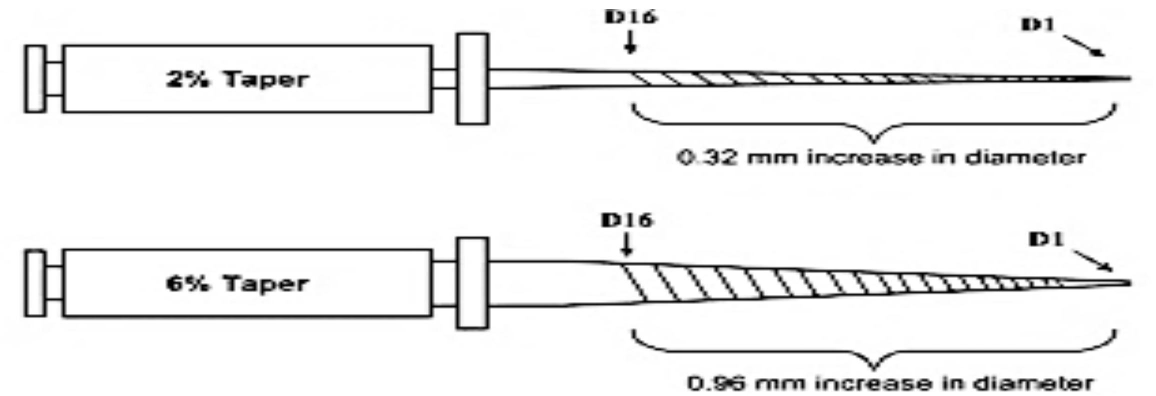


Figure 2.6. Taper of the instrument at 6% is greater than at 2%, with a greater increase in diameter at 16 mm away from the tip. From “The principles of techniques for cleaning root canals,” by Young et al., 2007, *Australian Dental Journal*, *52*(s1), p. s54.

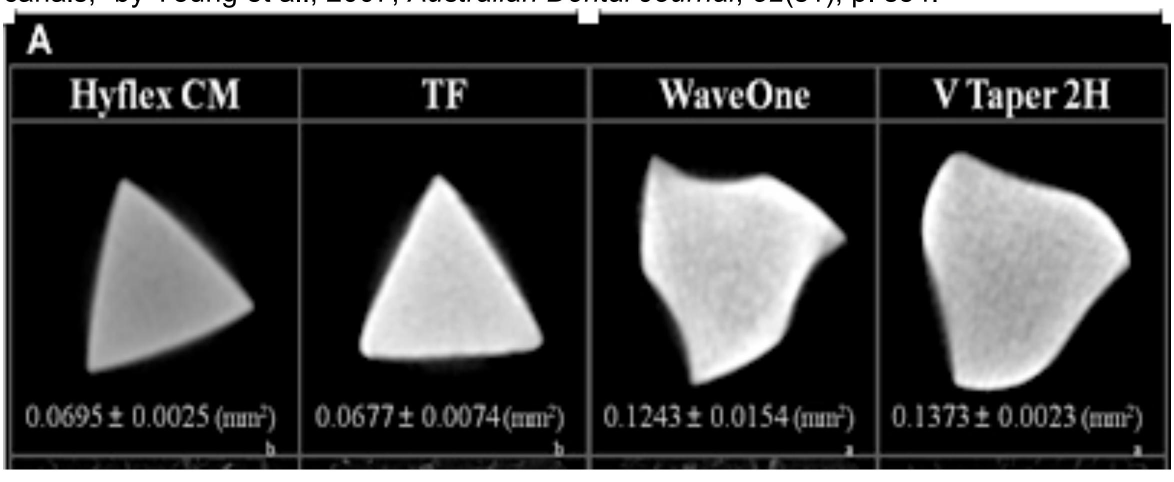


Figure 2.7.The variation of cross sections of four different files showing the cross sectional area (mm^2) at a 3-mm level from the apical tip of each rotary file. From “Various heat-treated nickel–titanium rotary instruments evaluated in S-shaped simulated resin canals,” by Gu et al., 2017, *Journal of Dental Sciences*, *12*(1), p. 17.

A file with a triangular cross section may have more resistance to cyclic fatigue than one with a square cross section; the triangular shape allowing three points of contact whilst square would create four contact points in the canal (Capar, Ertas & Arsalan, 2014; Uygun et al., 2016). A square cross section has greater bulk than a circular cross section making the file stiffer (Khasnis et al., 2018). An off-centred design, is when the axis of rotation is not in line with the geometric cross sectional centre, reduces stresses on the file by reducing contact and creating space for debris removal and is seen in files like ProTaper Next and WaveOne Gold^{TM} (Webber, 2015; Ha et al., 2017) to improve cyclic fatigue resistance (Capar & Arsalan, 2016; Ha et al., 2017).

Non-cutting tips prevent the tip of the file becoming stuck or locked in and factors such as pitch, radial lands, rake angle and helical angle can affect fatigue resistance (Khasnis et al., 2018). Pitch is the number of spirals per unit length of the file, so the longer the length of the pitch or smaller the pitch (Figure 2.8) the less are the chances of the file screwing into the canal (Sanghvi & Mistry, 2011; Khasnis et al., 2018). Versluis, Kim, Lee and Lee (2012) found that a decreasing pitch length or more spirals were associated with reduced flexural stiffness or resistance to bending and that a square cross section was stiffer than rectangular and triangular cross sections.

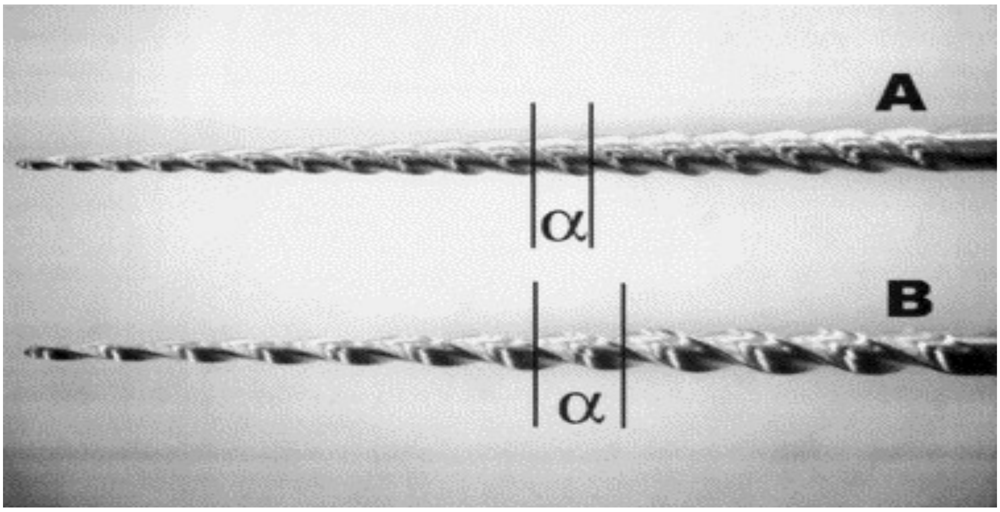


Figure 2.8. Differences in Pitch length, File A with a shorter pitch length, than in file B marked by lines corresponding to α. From “Effect of pitch length on the behaviour of rotary triple helix root canal instruments,” by F. Diemer and P. Calas, 2004, *Journal of Endodontics*, 30(10), p. 716.

The radial lands or blade support is the amount of material supporting the cutting edge, so the less support, the less resistance to torsional failure (Sanghvi & Mistry, 2011).

Rake angle gives the file cutting efficiency and is the angle the cutting edge makes with a cross section taken perpendicular to the long axis of the instrument (Figure 2.9); with a positive rake angle giving a more digging in effect and less torsional resistance (Sanghvi & Mistry, 2011; Khasnis et al., 2018).

Figure 2.9. The Rake angle, the image on the left showing cross section of file and green line outlines the negative rake angle and on the right positive rake angle. From "Descriptions of protocols and terminology, Introductions and Descriptions, Mastering Endodontic Instrumentation: An Online Addendum," by J.T. McSpadden, 2015, (https://nanoendo.com/blog/descriptions-of-protocols-and-terminology/).

The helical angle (Figure 2.10) is the angle the cutting edge makes with the long axis of the file, with variable angles allowing for greater debris removal and the file will be less likely to screw into the canal (Sanghvi & Mistry, 2011; Khasnis et al., 2018).

Figure 2.10. The helical angle highlighted by the green line on file. From "Descriptions of protocols and terminology, Introductions and descriptions, Mastering Endodontic Instrumentation: An Online Addendum," by J.T. McSpadden, 2015, (https://nanoendo.com/blog/descriptions-of-protocols-and-terminology/).

2.1.3. The surface treatment of the file

The surface of the file can be rough, which can have an effect on crack initiation, as the rough areas act as areas for debris to accumulate, causing areas of stress concentration, which leads to the propagation of a crack (Anderson et al., 2007; Kim, Yum, Hur & Cheung, 2010). When an instrument is machined, plastic deformation occurs at the surface where residual stresses remain; if these stresses are compressive, they prevent crack propagation but tensile stresses increase propagation and reduce fatigue resistance (Kim et al., 2010). Electropolishing removes surface defects as seen in RaCe™ files but although several studies showed improved properties, some showed that it could not prevent the development of cracks (Kim et al., 2010; Chi, Deng, Lee & Len, 2017). Electro-discharge machining is a process of non-contact thermal erosion of wire by spark discharges, can create a harder surface which is seen in the Hyflex EDM file (Iacono et al., 2017). Some files have surface treatments and coatings which make them smoother like Vortex Blue has a thicker titanium oxide coating (Plotino, Grande, Cotti, Testarelli, & Gambarini, 2014; Gavini et al., 2018). Coating files with a layer of glass may increase their cyclic fatigue resistance by preventing the initiation of cracks (Chi et al., 2017).

2.1.4. The torque applied to an instrument

Gambarini (2000) describes torque as the twisting force applied to the instrument, which is seen as unwinding of the file before fracture occurs. Motors are set to the limit of torque that can be applied to an instrument, which is close to the limit of elasticity at which point the motor stops. Pedulla et al. (2015) and Asthana, Kapadwala and Parmar (2016) mention that torsional fatigue can also occur due to frictional resistance on the walls of the canal. This can occur if a large surface of the instruments rubs excessively against the canal wall, when the tip is larger than the canal or if the practitioner applies too much force. This can be prevented by using a gentle pecking motion when placing a rotary file in the canal (Ferreira et al., 2017). Martensitic files show signs of torsional fatigue by unwinding and increasing in length, which can be recognised by the practitioner (Singh & Kapoor, 2016).

2.1.5. The movement of the file

The rotary file can move in continuous rotation or in reciprocation, depending on the settings of the motor and recommendations of the manufacturer. Reciprocation is when the file twists by a certain amount clockwise and then twists back a certain degree anticlockwise and so never completes a full circle in one cycle (Figure 2.11 & 2.12). Several studies have shown that files which are used in a reciprocating action have a higher cyclic fatigue resistance than those used in continuous rotation (Gambarini, Gergi, Naaman, Osta & Al Sudani, 2012; Cunha, Junaid, Ensinas, Nudera & Da Silveira Bueno, 2014; Ferreira et al., 2017). Ferriera et al. (2017) suggested in a systematic review, that files used in reciprocation seem to have better cyclic fatigue resistance than those used in continuous rotation, like Hyflex CM but it did not include any studies of the martensitic files, like Hyflex EDM, which are used in continuous rotation.

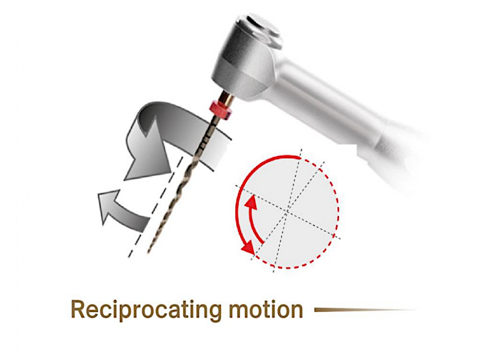


Figure 2.11. Reciprocation. From “WaveOne: Reciprocation,” by W.B. Johnson, 2011, (http://endomatters.dental/waveone-reciprocation/).

Figure 2.12.The movement of files in reciprocation (left) and continuous rotation (right) as marked by arrows. From “Can Reciprocating files replace rotary files?” by S. Goutham, 2017, (https://pinkblue.in/blog/can-reciprocating-files-replace-rotary-files/).

2.1.6. The instrument technique

A multiple file system would distribute the stresses over the several files used but a single file system would be used for longer and concentrate all stresses on the one file used, increasing the risk of fracture (Ahn et al., 2016; Arias et al., 2017). Dhingra and Neetika (2014) define a glide path as the creation of a smooth tunnel from the top of the canal to the end of the canal. This involves the use of files from smaller to larger, in a sequence to enlarge the canal creating a tapered funnel shape. The use of a glide path creates space for the next file which prevents stresses and binding of the file to the canal walls. Early coronal flaring removes obstructions, creates straight-line access and reduces fatigue on the instruments (Gutmann & Fan, 2016).

2.1.7. The skill of the operator

It has been mentioned that experienced dentists have less instrument separation, as they are more comfortable with using higher torque settings and recognise signs of instrument deformation quickly (Cunha et al., 2014). Endodontists report a file separation incidence of 0.13% (Cunha et al., 2014) to 5 % (Terauchi, 2016). In the author’s opinion, this can be an area of considerable variation and subject to interpretation. Operator fatigue and too much apical pressure during instrumentation can be reasons for instrument separation.

2.1.8. The speed of the file

The rotary file usually has a certain number of rotations, after which fracture occurs (Khasnis et al., 2018). Different files are used at different speeds according to the manufacturer’s guidance but the speed at which the instrument rotates can be a factor limiting the length of time a file is used (Koch & Brave, 2006). Ha, Kwak, Kim, Sigurdsson and Kim (2017) showed that the torsional resistance of files in in vitro tests were unaffected by the speed of rotation. Lopes et al. (2009) showed that the cyclic fatigue resistance decreased in Protaper™ files when the speed of rotation increased but Gao, Shotton, Wilkinson, Phillips and Johnson (2010) showed that the speed of rotation had no effect on the cyclic fatigue resistance of Profile Vortex™ files.

2.1.9. The presence of irrigants or debris

Irrigants act to lubricate files but can cause corrosion. This may be a problem in countries where files are reused, as it can shorten the cyclic fatigue resistance (Young et al., 2007) but this should not be considered a problem in the United Kingdom and Germany, as a single use policy has been adopted (Azarpazhooh & Fillery, 2008). It could be a problem, if the same file is used in more than one severely curved canal, for example, when clinicians use one file for all the canals in a molar tooth. Debris may accumulate in the canal with a single file system more quickly, clog up cracks or surface defects and lead to crack propagation (Figure 2.13). Wealleans, Kirkpatrick and Rutledge (2011) showed that electropolishing did not increase the cyclic fatigue resistance of Endosequence™ files in the presence of dentine debris.

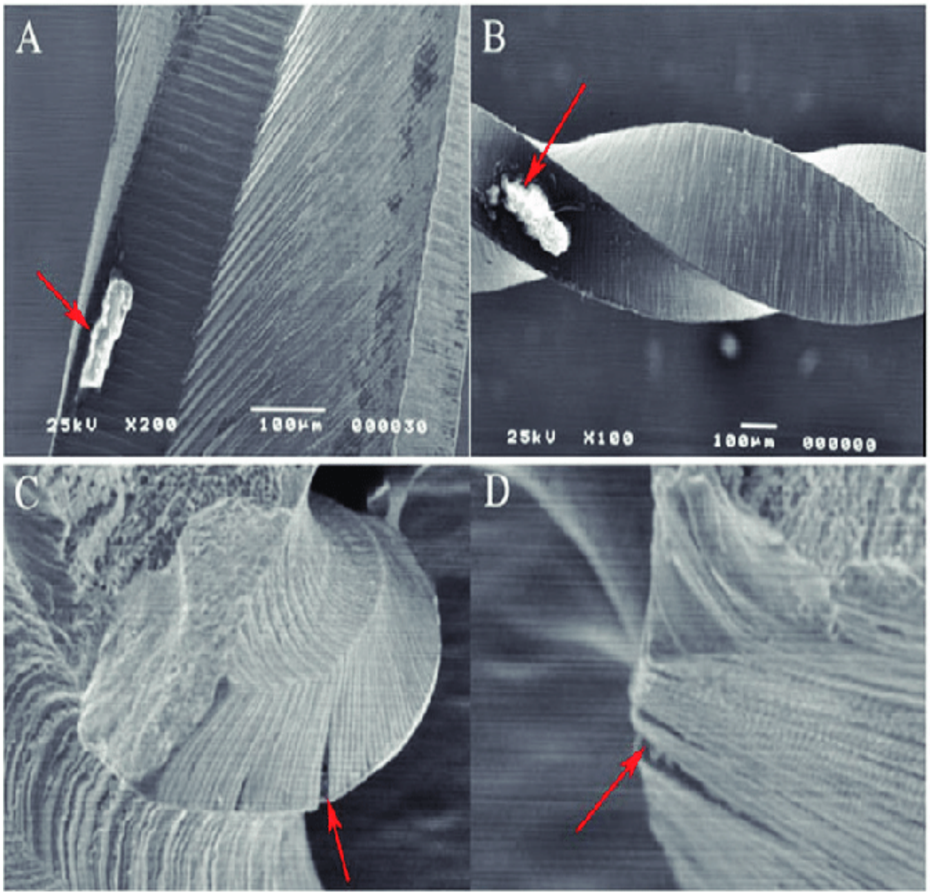


Figure 2.13. Debris in ProTaper Universal™ and ProTaper Next™ file indicated by red arrows in pictures A and B, showing crack formation and initiation of fracture indicated by red arrows in C and D. From “Analysis of Surface Characteristics of ProTaper Universal and ProTaper Next Instruments by Scanning Electron Microscopy,” by Bennett et al., 2017, *Journal of Clinical and Experimental Dentistry*, 9(7), p. 881.

2.1.10. The type of alloy

NiTi alloy can vary in its composition, with variation in the amount of nickel and titanium; slight modifications in the ratio can change the properties of the alloy, for example, Hyflex CM files have 52.1% by the weight of nickel (De Arruda Santos, De Azevedo Bahia, De Las Casas & Buono, 2013) with the surface layer having 13% nickel and 35% titanium whilst the surface layer of Hyflex EDM files has 45.6% titanium and 27.5% nickel as seen in Appendix D (Iacono et al., 2017). The alloy has three states which are austenitic, martensitic and R-phase (Shim et al., 2017) and can have a combination of these phases but it is the percentage of the dominant phase that will determine its properties (Zupanc et al., 2018). NiTi can exist in a martensitic phase which is a low temperature phase, having a B19′ crystal structure; or an austenitic structure which has a cubic B2 structure and is the high temperature phase (Aoun et al., 2017; Zupanc et al., 2018). The B2 structure or austenite has the atoms arranged in a cube with nickel atoms occupying a central position in the cube making it body centred (Figure 2.14); whilst in the B19′ structure or martensitic structure the atoms have an appearance which is more twisted, with the nickel atoms not directly in line with each other, giving a face centred or hexagonal close packed lattice (Santoro, Nicolay & Cangialosi, 2001). The distorted structure of martensite allows the material to be deformed to a greater extent in clinical situations than austenite (Aoun et al., 2017).

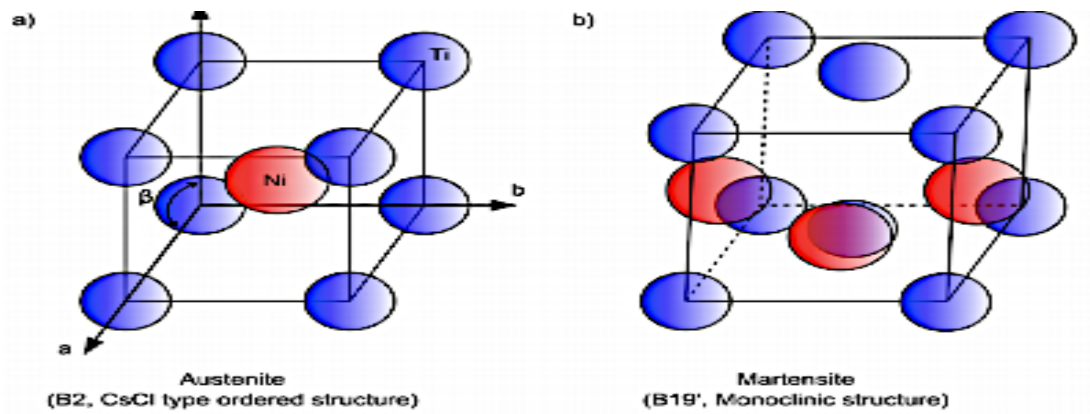


Figure 2.14. The structure of NiTi a) B2 structure or body centred structure of austenite b) B19 structure or face centred structure of martensite with Nickel represented as red balls and Titanium as blue balls. From “Introduction to Nitinol” by Memry Cooperation, 2017, (https://daks2k3a4ib2z.cloudfront.net/59fcbaf103e295000131288b/5a4bb3895344bc000191bac9_Introduction%20to%20Nitinol_V5.pdf).

2.1.11. The manufacturing process

Certain procedures, like aging at high temperatures of 400 °C, the addition of another element like aluminium or iron, or heat treatment after cold working, can cause the formation of the R-phase (Zupanc et al., 2018). The R-phase forms between the transition from austenite to martensite on cooling, or martensite to austenite on heating (Figure 2.15). The R-phase is a distorted phase and is considered to be a variant of the martensitic phase (Hieawy, Haapasalo, Zhou, Wang & Shen, 2015). It has a simple hexagonal lattice or network arrangement of nickel and titanium atoms (Santoro et al., 2001). As the alloy is cooled, the temperature at which the R-phase starts to form is the R_s and the temperature at which the phase finishes forming is the R_f.

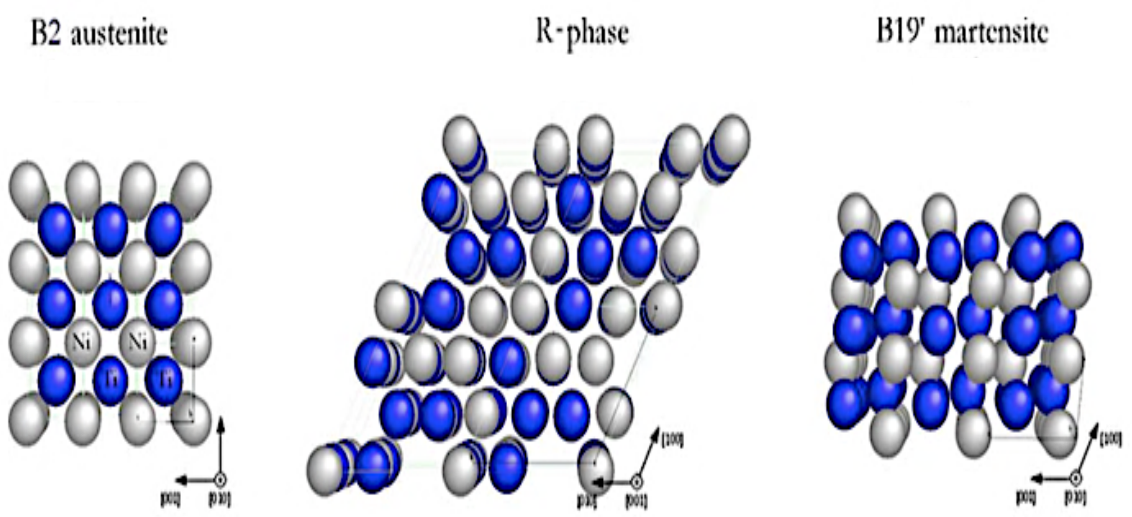


Figure 2.15. Structures of NiTi: B2 austenite, R-phase and B19′ martensite. Ni and Ti atoms are shown as grey and blue coloured spheres respectively. By D. Prace, 2014. (https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcSP8tEJqKpHWKwvqYBkgUN7fSb0ITnV5FMqx8Qoay-S_fadGany).

There are two ways the phases can be changed:

1. The alloy can be changed from one phase to the next by heating or cooling.
2. The phase change can occur by the application of stress.

NiTi alloy has two properties, which are superelasticity and shape memory. When NiTi alloy, which has superelastic properties, has stress applied to it, it can cause the change in phases from austenite to martensite, which can accommodate up to 8% strain or deformation, forming stress induced martensite, which is unstable and recovers when the stress is removed (Laplanche, Birk, Schneider, Frenzel & Eggeler, 2017; Zupanc et al., 2018) (Figure 2.16). This is called superelasticity or psuedoelasticity which is mostly found in austenitic NiTi (Zupanc et al., 2018). The strain can be elongation or deformation of a material that has been subjected to force. Kimiecik, Jones and Daly (2013) and Carvalho et al. (2015) mention that the strain accommodated can be up to 10% but Kimiecik et al. claim that different areas of the NiTi alloy can have different amounts of strain, so it is not uniformly spread across the alloy.

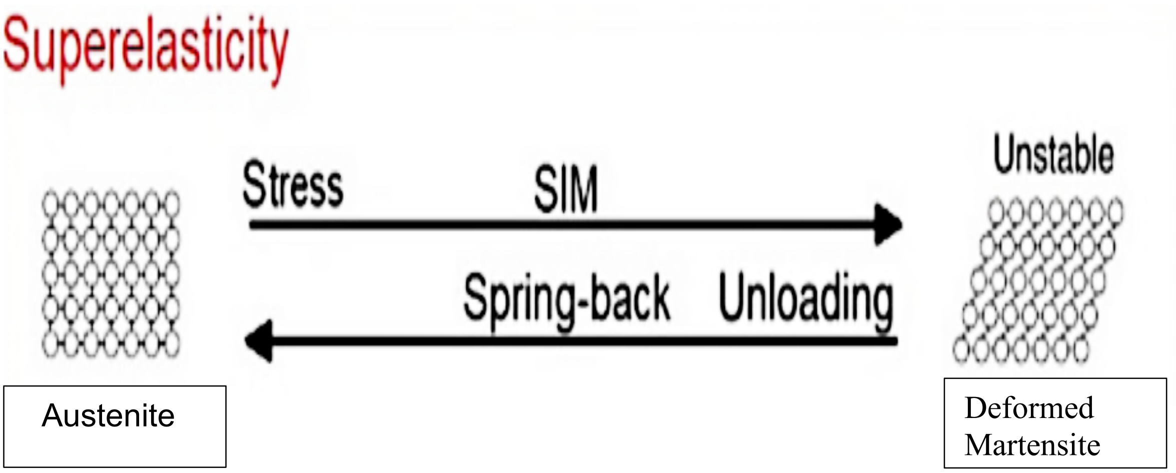


Figure 2.16. Phase transformation with superelasticity when the material is austenitic, SIM or stress induced martensite is unstable and springs back on the removal of the force. Adapted from "New thermomechanically treated NiTi alloys - a review," by Zupanc et al., 2018, *International Endodontic Journal*, 5 (10), p. 1090.

When NiTi is heated, the temperature at which the martensite structure first starts to change to austenite is called the austenite start temperature or A_s and the temperature at which this process is complete is the austenite finish temperature or A_f. On cooling, the temperature at which martensite starts to form from austenite is called M_s or the martensite start temperature and the temperature at which martensite finishes formation is called M_f or martensite finish temperature.

From the graph (Figure 2.17), it can be seen that these four temperatures are different and a range exists between these temperatures where the alloy will be in a mixture of phases (Zupanc et al., 2018). Factors can affect the transition temperature of the alloy, which at intracanal temperature, can exist as either austenitic, martensitic, R-phase or a mixture of the phases.

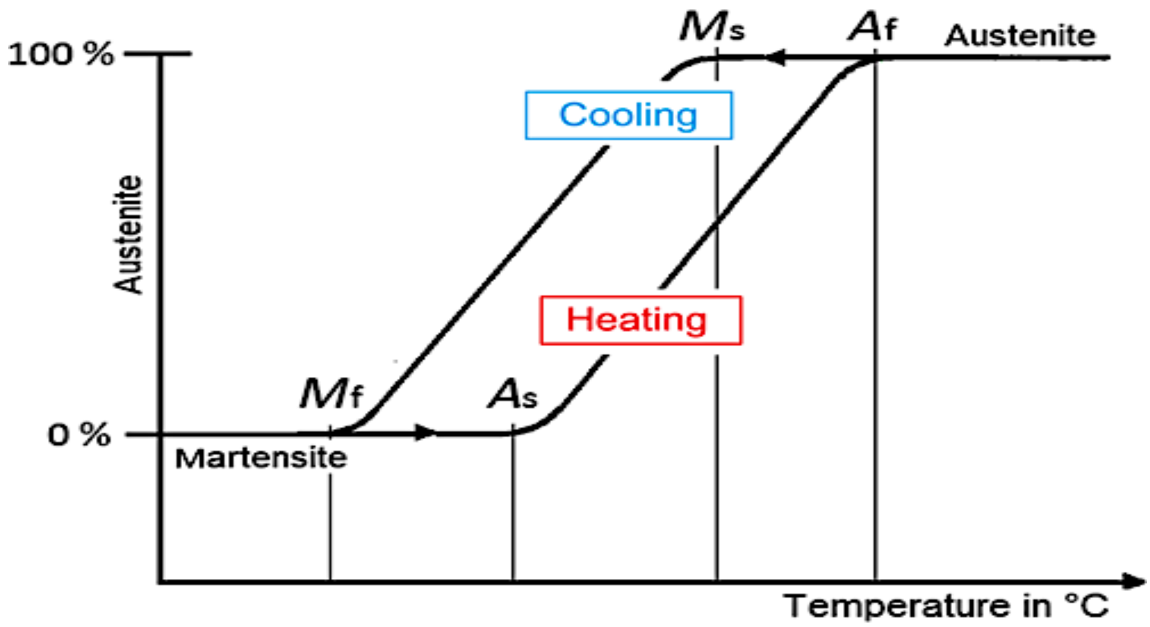


Figure 2.17.The transition temperature of NiTi alloy and transformation from austenite to martensite and vice versa, martensite start temperature (M_s), martensite finish temperature (M_f), austenite start temperature (A_s), austenite finish temperature (A_f). From “New thermomechanically treated NiTi alloys - a review,” by Zupanc et al., 2018, *International Endodontic Journal*, 5(10), p. 1090.

The second property is shape memory, which is the ability of NiTi to recover to its original shape when heated, due to the phase changing from stable deformed martensite to stable austenite (Zupanc et al., 2018). The alloy with this property, has a martensitic finish temperature which is higher than room temperature, so the alloy is in a martensitic state (Figure 2.17). When stress is applied, it forms twinned martensite or other varieties of martensitic phases, like R-phase, with subsequent reorientation to form a stable martensite phase (Figure 2.18). Martensite can have a number of variations with complex interactions during the phase changing process (Kimiecik et al., 2013). The alloy can change directly from B2 to B19′ or have an intermediate phase, like R-phase, with each individual region having different combinations of these martensitic phases (Kimiecik et al., 2013).

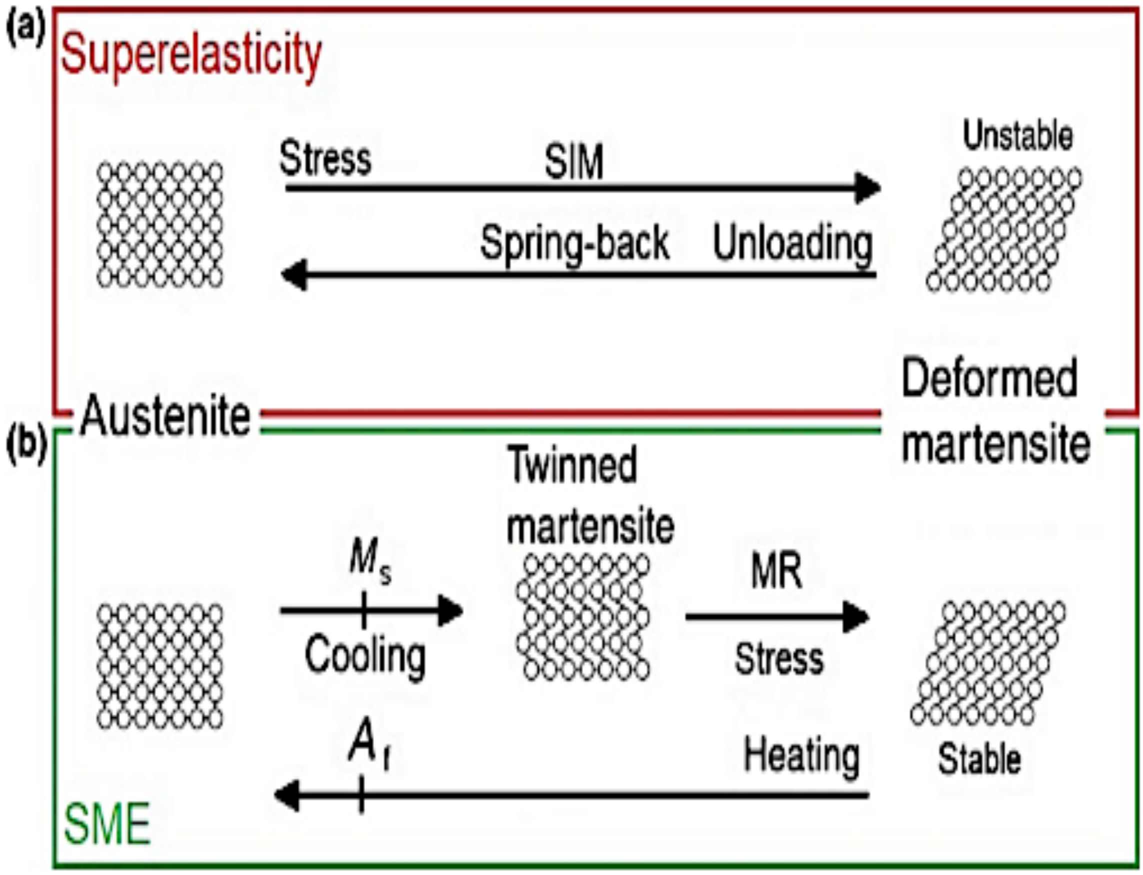


Figure 2.18. Martensitic transformation with a) Superelasticity when the ambient temperature is above A_f, SIM or stress induced martensite is unstable and springs back on the removal of the force, b) SME or shape memory effect when the ambient temperature is below the martensite finish temperature with MR or martensite reorientation needing less stress than SIM. From “New thermomechanically treated NiTi alloys - a review,” by Zupanc et al., 2018, *International Endodontic Journal*, 5(10), p. 1090.

The process of manufacture involves heating the file above the A_f, when the instrument is in the austenitic state. As it cools, an austenite to martensite transformation occurs at M_s with a B2 to B19′ transformation of the crystal structure but the martensite or B19′ structure is stressed. The stress is released by twinned martensite forming a stable martensite, which can be deformed up to 8% forming a stable phase, when stress is applied to the file it bends, similar to the stress induced martensite in a more austenitic file but it differs that it maintains its shape once the stress is removed (Figure 2.16). This gives the ability of a martensitic phase file to be pre-curved; with the phase being soft, ductile, flexible and having a low modulus of elasticity. The modulus of elasticity is the measure of the resistance of a material to being deformed non-permanently when stress is applied; a stiffer material will have a higher modulus of elasticity as seen in austenitic NiTi files. The more martensitic the file is at the intracanal temperature the greater its flexibility and resistance to cyclic fatigue (Campbell et al., 2014; Terauchi, 2016) but the phases are complex, with some studies identifying several types of martensitic phases (Kimiecik et al., 2013).

2.12. Intracanal temperature

The temperature within the canal is not room temperature, with factors like dentine thickness or the presence of irrigant, affecting temperature. Most cyclic fatigue studies are conducted at room temperature, with no consideration of intracanal temperature. Room temperature is about 20 ± 2 °C (Grande et al., 2017), whilst intracanal temperature has a variable range of 31 °C to 37 °C, with the canal coronally being cooler at 31- 33 °C and apically warmer (De Hemptinne et al., 2015). The intracanal temperature can be near body temperature at 35 - 37 °C (De Hemptinne et al., 2015), with temperature having an influence on the phases present in the alloy during its use.

Zupanc et al. (2018) stated that several studies showed that increasing the environmental temperature from room temperature to intracanal temperature decreases the cyclic fatigue resistance. Grande et al. (2017) showed that lowering the temperature to -20 °C, using a tetraflouroethane spray, in in vitro tests could increase the cyclic fatigue resistance of various files significantly. A recent randomised control trial by Vera et al. (2018) shows the effects of cold or cryotherapy in the canal, reducing the incidence of post-operative pain in patients having pre-operative pain. This trial used saline at 2.5 °C to irrigate the canal with reference to previous studies, where the cold effect lasted for 4 minutes when the temperature was measured at the root surface.

2.2. Is cyclic fatigue more important than other types of fatigue?

Sattapan, Nervo, Palamara and Messer (2000) claimed that torsional fracture occurred in 55.7% of the files studied and cyclic fatigue occurred in 44.3% of files. However, the study used files which had been discarded after being used several times in specialist practice, either due to visible signs or reduced efficiency, with 50% of them having visible signs of deformation, like unwinding, which are regarded as signs before torsional failure occurs. The imaging of the files used a magnification of 22x, rather than the more recent imaging techniques, which look at the cross section of the fractured ends at much higher magnifications (Figure 2.19), so the study may have incorrectly overestimated fracture by torsion. Cheung, Peng, Bian, Shen and Darvell (2005) claimed that 93% of instrument separation was due to cyclic fatigue.

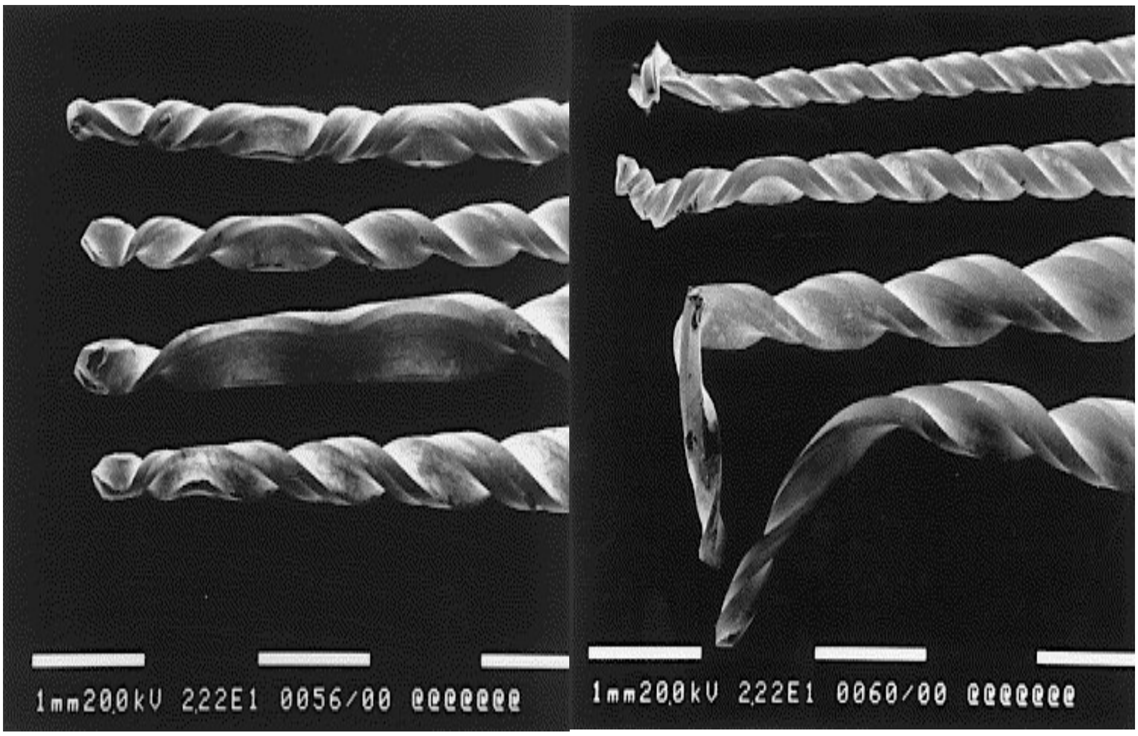


Figure 2.19. Files showing visible signs of deformation, unwinding on the left and on right other defects like bending. From “Defects in rotary nickel-titanium files after clinical use,” by Sattapan et al., 2000, *Journal of Endodontics*, *26*(3), p. 164–165.

Cross sectional images of fractured areas under scanning electron microscope or SEM, magnifies the area, looking for striations or lines across the fractured surface in the form of dimples or craters. A fracture by torsion (Figure 2.20) has a more central mark which has a torn or twisted appearance, with higher magnifications showing a larger twisted dimple in the centre but a surface that has fractured by cyclic fatigue has striations and dimples scattered on its entire surface (Figure 2.21) (Kim et al., 2010, Goo et al., 2017).

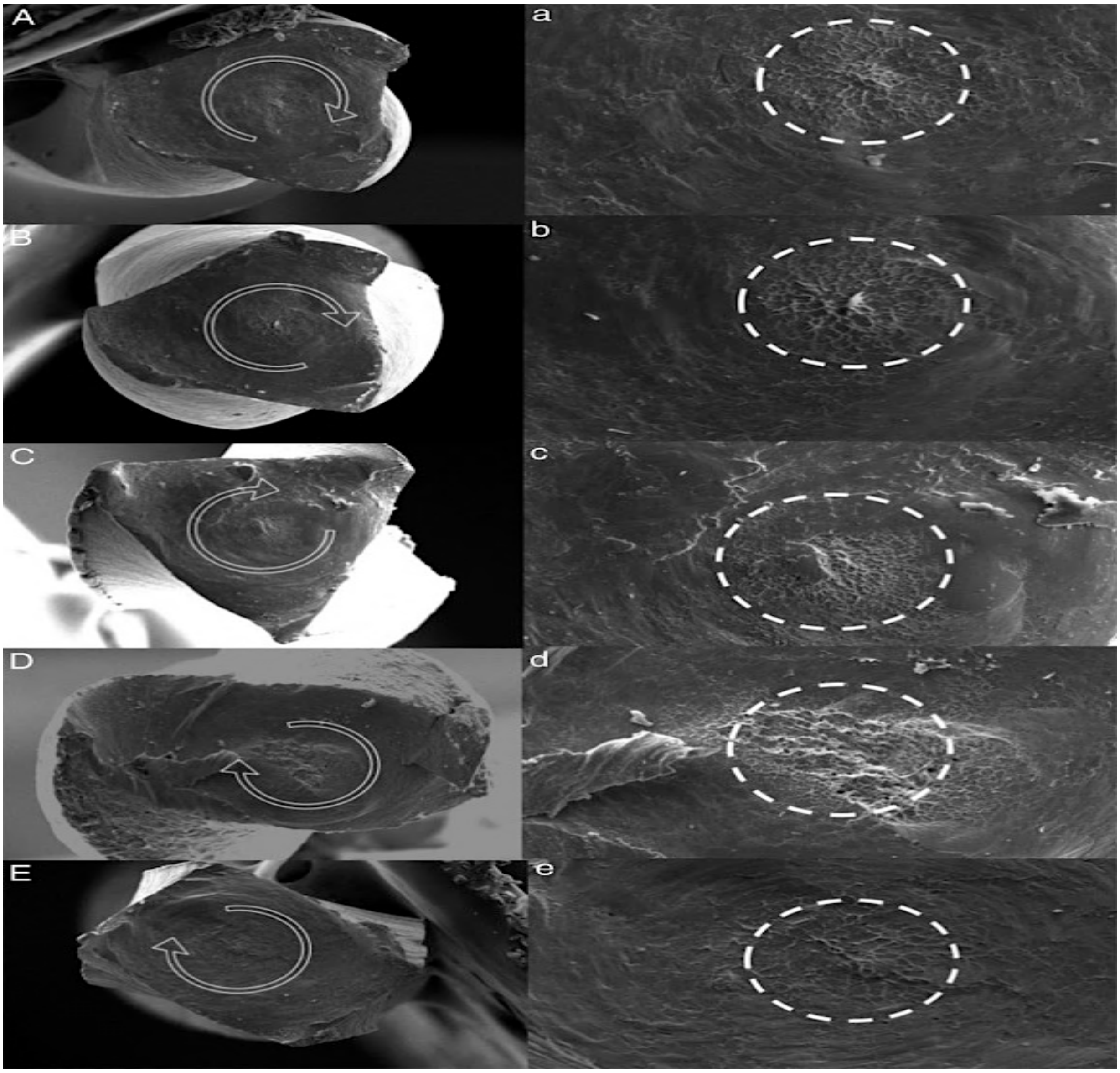


Figure 2.20. SEM images of torsional fracture with cross sectional fractured surfaces of various files A-E at magnification x200, whilst a-e is at x500. The circular arrows on the left indicate the circular abrasion marks and dotted circles on the right show skewed dimples in the central area of rotation at higher magnification. From “Mechanical properties of various heat-treated nickel-titanium rotary instruments,” by Goo et al., 2017, *Journal of Endodontics*, *43*(11), p. 1875.

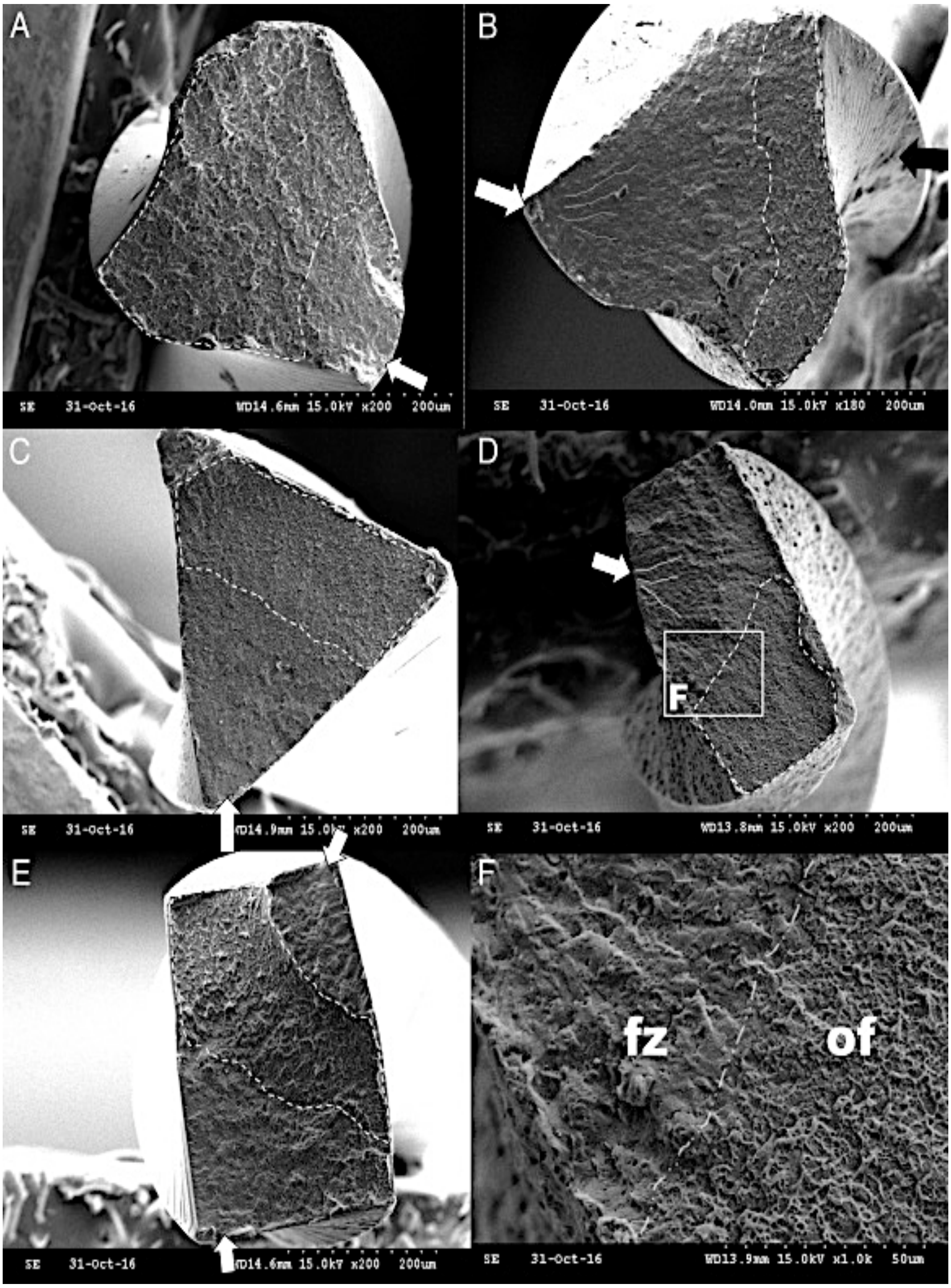


Figure 2.21. SEM images of instruments separated by cyclic fatigue. Images A-E has magnification x200 and Image F is x1000. White arrows indicate the point where the crack has started, then the white dotted area showing an area of fast fracture zone or fz. In Image F, the OF, or overload fracture zone has numerous small dimples. Cyclic fatigue shows striations and dimples throughout the surface. From “Mechanical properties of various heat-treated nickel-titanium rotary instruments,” by Goo et al., 2017, *Journal of Endodontics*, *43*(11), p. 1874.

2.3. Problems with Cyclic fatigue testing

There has been no international standard established for testing of cyclic fatigue resistance in instruments, which can make comparison of the studies which use different testing methods difficult (Plotino, Grande, Cordaro, Testarelli & Gambarini, 2009; Cho, Versluis, Cheung, Ha, Hur & Kim, 2013; Carvalho et al., 2015). The tests are designed to simulate canal curvature, which Schneider first defined in 1971. He drew a line along the long axis of the coronal portion of the root, a second line was drawn from the foramen or apex of the tooth to intersect the first line, with the acute angle formed between both the lines measured as shown in Figure 2.22 (Plotino et al., 2009). Problems with this method are the lack of clarity, as to whether the lines should touch the canal or the root surface, as this will give different measurements (Figure 2.22).

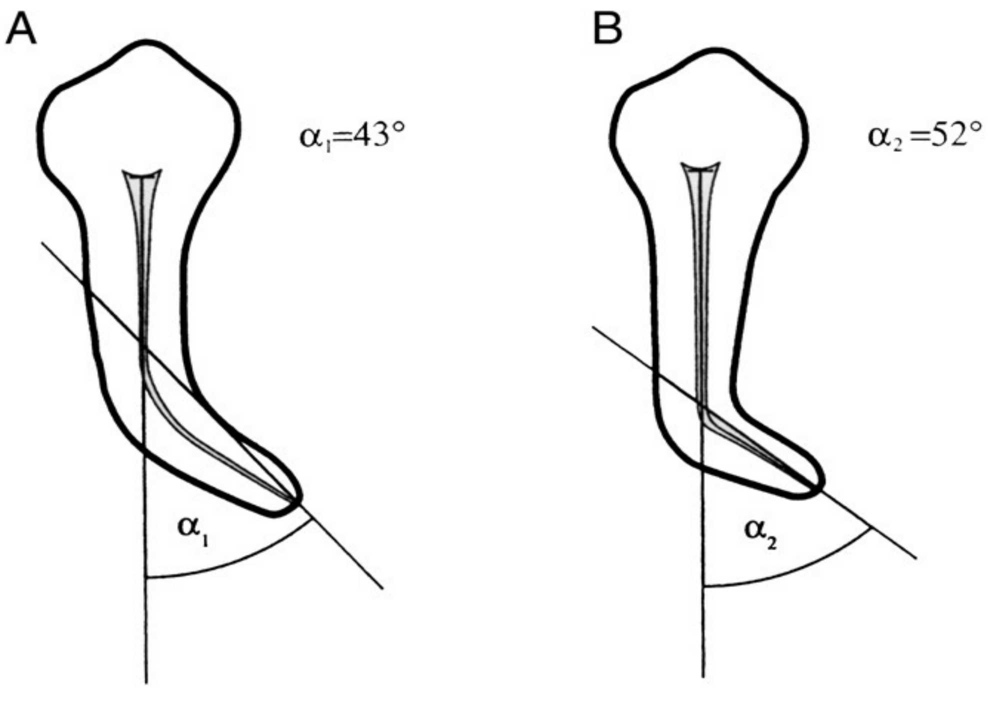


Figure 2.22. Problems with methods of measuring the degree of curvature in Schneider's method. Two lines are drawn along the long axis of the coronal portion of the tooth and the long axis of the root . The angle α is measured between these two lines but the line from the foramen can be along the canal or touching the root surface which gives different measurements on the same tooth. In A) the angle $\alpha1$ is 43° and in B) $\alpha2$ is 52°. From "Cyclic fatigue testing of nickel–titanium endodontic instruments," by Pruett et al., 1997, *Journal of Endodontics,* 23 (2*),* p. 78.

Pruett, Clement and Carnes (1997) measured the curvature using two numerical measures, an angle of curvature and a radius of curvature. The angle of curvature is measured on the side of the curve by drawing an arc which contacts two points of the lines drawn in Schneider's method, which are in contact with the canal, whilst the radius of the arc is the second numerical measure and this is more important in determining the risk of instrument separation as shown in Figure 2.23 (Pruett et al.,1997; Plotino et al., 2009). The radius gives information on whether the curvature is abrupt or gradual, the abrupt curvature having a smaller radius. A further addition has been the distance of the curvature from the root tip which gives the location of the curve. This method cannot be applied to the canals which can have a double or S-shaped curve, as the second curve may not be in the same plane as the root curvature.

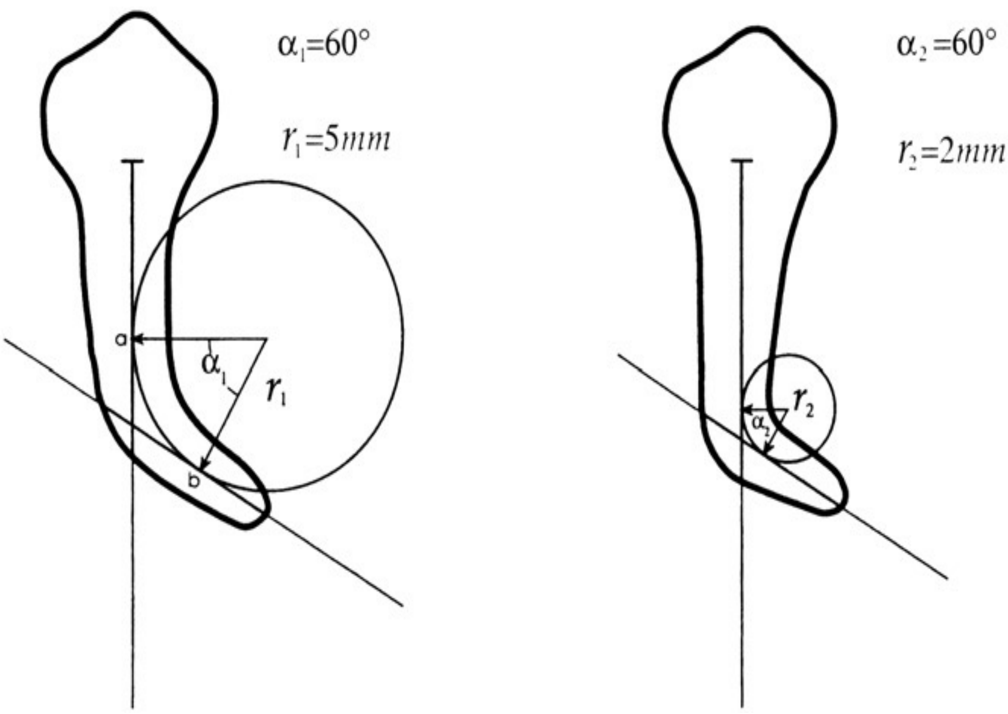


Figure 2.23.The curvature is measured by two parameters. The angle α is measured by drawing an arc which touches the two lines drawn along the long axis of the tooth. Both teeth have the same angle .The radius r is the second parameter, r_1 is 5 cm, a smaller radius r_2 is 2 cm means a more abrupt curvature in the Pruett method. From "Cyclic fatigue testing of nickel–titanium endodontic instruments," by Pruett et al., 1997, *Journal of Endodontics,* 23(2*),* p. 79.

Cheung (2009) mentions four types of testing methods, a curved tube, grooved block and rod, rotation against an inclined plane and the three-point bending test (Figure 2.24).

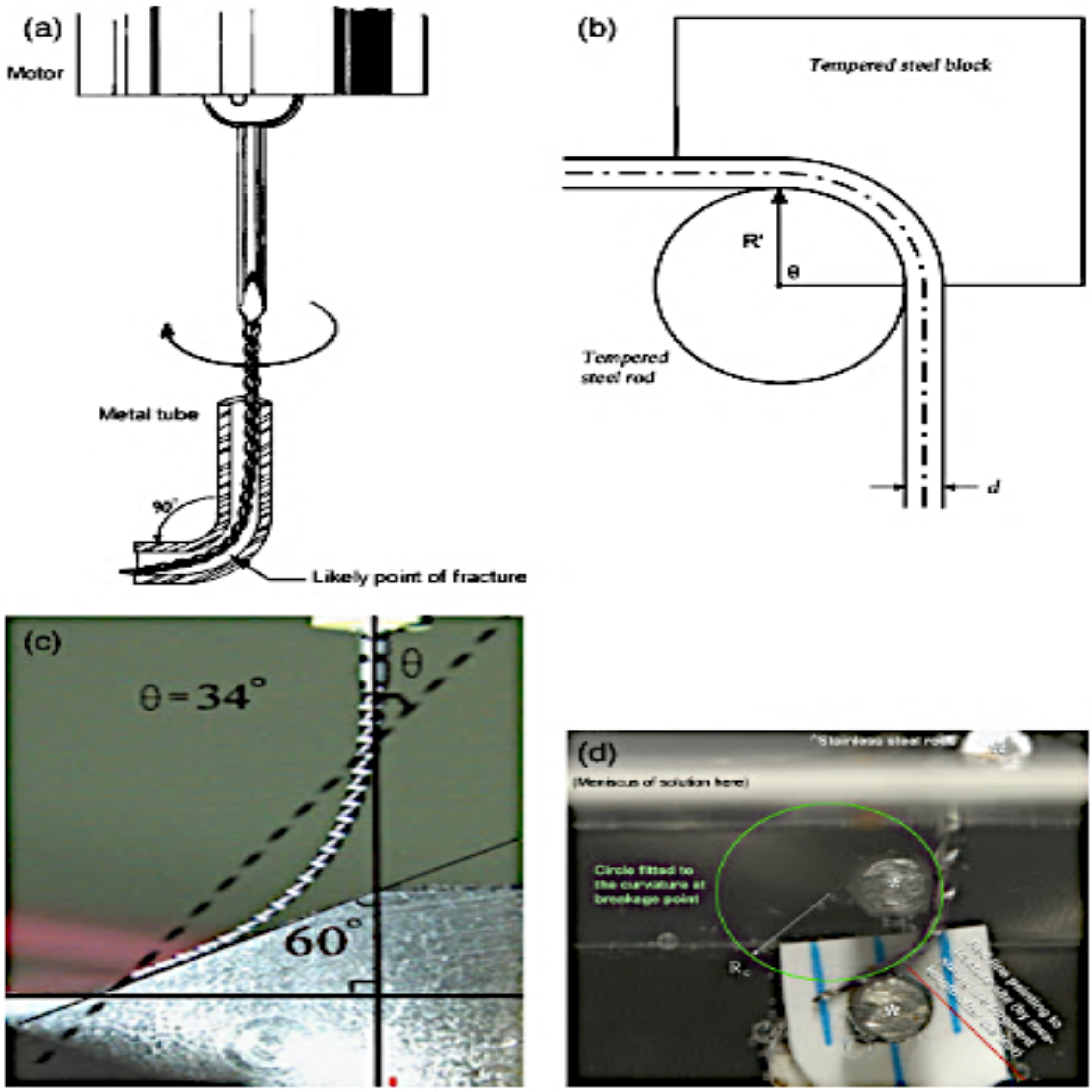


Figure 2.24. Various methods to test NiTi rotary files (a) curved metal tube (b) groove block-and-rod (c) inclined plane and (d) rotation in a three-point bend. From "Instrument fracture: mechanisms, removal of fragments and clinical outcomes' by G.S.P. Cheung, 2009, *Endodontic Topics*, *16*(1), p. 4.

Plotino, Grande, Cordaro, Testarelli and Gambarini (2009) describe various tests on cyclic fatigue resistance, which involve setting up an experimental system to bend a file, whilst it rotates in the hand piece. A tube of metal of a small diameter about 1.5 mm, can be curved to form a simulated curved canal. These hollow tubes can be made of different materials, like glass or metal, which can have different shapes, diameters or curvatures. However, problems with standardisation encountered in this method are that the NiTi file, being tapered, is not a uniform width throughout its length, so large portions of the file will be loose in the canal, causing the file to vibrate as it rotates and it is difficult to visualise the time when the file fractures if using a metal tube as shown in Figure 2.25 (Plotino et al., 2009; Cho et al., 2013).

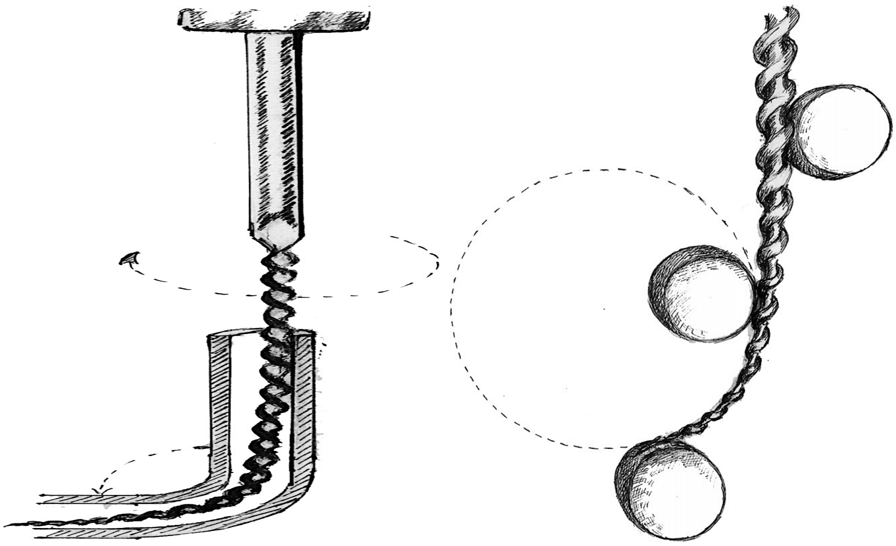


Figure 2.25. Diagram showing the drawing of the three-point bend testing with the file on the right side and the file in a curved metal tube test on the left side. From “A review of cyclic fatigue testing of nickel-titanium rotary instruments”, by Plotino et al., 2009, *Journal of Endodontics,* 35(11), p. 1471-72.

The three-bend testing method uses three pins, set along the length of a file, to create the three bends as shown in Figure 2.25 (Plotino et al., 2009; Carvalho et al., 2015). However, this system has the disadvantage that the sides of the file are not in contact continuously sideways as it may be in a canal, so it does not get any lateral force which would be similar to the constraints of a canal (Cho et al., 2013). The three pins need to be placed precisely but when comparing files of different tapers, this will still create different angles so cannot accurately compare them (Plotino et al., 2009). The inclined plane test is carried out by pressing the file against an inclined plane but this can produce a variation in the angle created compared to the angle of the plane (Cheung, 2009). The grooved block-and-rod consists of a V-shaped groove as the artificial canal in a steel block, having a size matched steel rod which constrains the file in the groove. However, unless the groove was matched to the instrument, the fit of the instrument in the groove can vary (Cheung, 2009). The best test, which is the fifth method, is to make custom fit canals for each taper of the file, which provides a better fit (Figure 2.26) but this is more expensive and time consuming (Plotino et al., 2009).

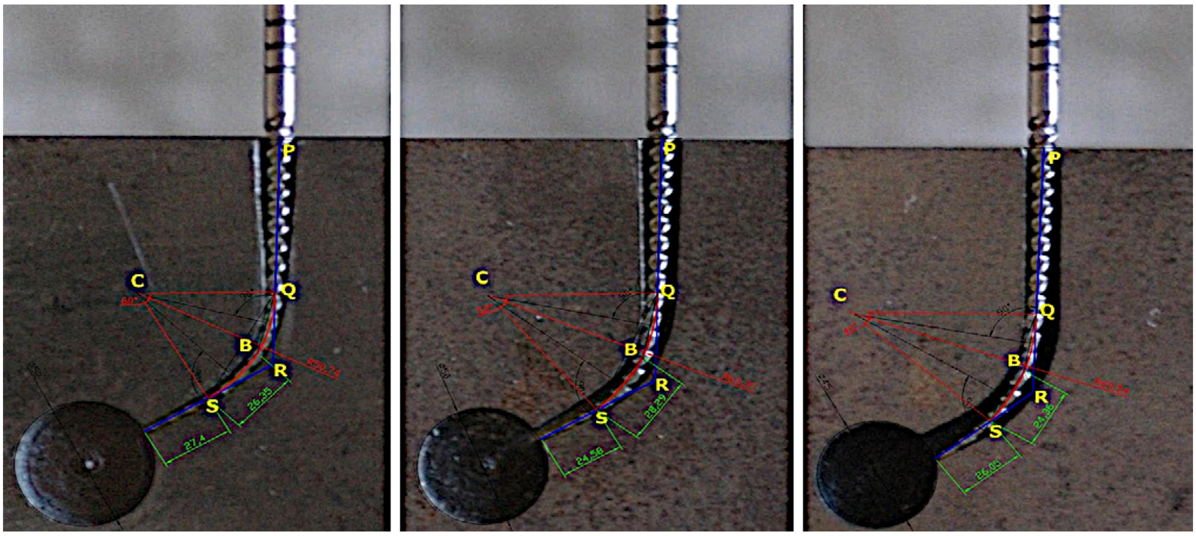


Figure 2.26. Picture showing a better fit of a custom canal (far left) and fits of the tapered file in a different tapered canal (middle) and untapered canal (right). From “A review of cyclic fatigue testing of nickel-titanium rotary instruments”, by Plotino et al., 2009, *Journal of Endodontics,* 35(11), p. 1475.

Further variations in the testing procedure is that the fracture of the files can be detected visually or audibly and the devices used to record this by the operator, such as a stopwatch, digital chronometer or a video recording, can vary precision. Operator fatigue can result in slower reaction times but studies using the three-bend testing system have allowed an independent measurement by a computer; an electric current goes through the system where once the file breaks the circuit is broken and the time is recorded accurately. If an experiment attempts using extracted teeth, also known as ex-vivo studies, it can be difficult to find similar canals and the tooth cannot be reused once the canal is enlarged (Plotino et al., 2009; Haapasalo, 2016). During the shaping process in a tooth, the fit of the canal changes as the file cuts the walls making it looser as it works but this is closest to the clinical situation and material being cut in clinical practice. This fit of the file in the canal and loss of fit as it enlarges the canal, could result in decreased need for resistance to separation, as the points of stress along the file change. The tests often use oil as a lubricant but to make it similar to clinical conditions, sodium hypochlorite which is commonly used in the cleaning and shaping process within the canal, should be used in the experiments (Plotino et al., 2009). Wealleans et al. (2011) stated that the effect of dentine debris on the fatigue resistance had not been investigated and showed that the electropolished surface of the files in the presence of dentine debris did not perform better. Most tests involve the use of metal against metal, causing friction which can increase the temperature of the file, causing a change in the metal phase that may not occur in clinical conditions (Lopes et al., 2009) and if sodium hypochlorite is being used may cause corrosion.

In the author's opinion, for dynamic tests using some dentinal fine particles or chips can also make the in vitro test similar to clinical conditions and using intracanal temperature. Instead of metal tubes, a material which is similar to dentine can be used for example, Haeri and Goldberg (2014) describe an acrylate polymer with tubular sub-structure or scaffold as a substitute for dentine in simulations. This material or a resin-based material could be a suitable substitute to simulate clinical conditions as it may provide less resistance to cutting than steel or ceramic and may create some debris similar to the clinical situation. The tests need to have dynamic and static parts; static creates a better comparison but dynamic conditions simulate clinical conditions, changes in stress as the file moves in and out of the canal and can consider the effect of temperature changes that can occur even for as little as a minute if heated irrigants are used. The complex anatomy of canals cause different stresses on the files, for example, when a file tip turns back into an adjacent canal, when canals join or communicate with each other. Current testing methods do not take this into consideration. In the author's opinion, as cyclic fatigue tests are in vitro with variation in the testing methods, it is difficult to translate this information and know precisely the limit on the number of rotations of a file until it fractures in a clinical situation, where torsion and cyclic fatigue occur simultaneously.

Methodology

3.1. Research methodology

This section will describe the methods used to carry out the review. In an attempt to follow a guideline for a systematic review, identifying a set of beliefs to use for research is helpful. A paradigm means a set of beliefs or world view (Bryman, 2004; Parahoo, 2006); in the past, most scientific research has followed a positivist paradigm, which means that only a certain reality exists that can be found and measured. Cochrane systematic reviews follow a quantitative and positivist approach from using randomised controlled trials to meta-analysis for quantitative analysis.

Bryman (2004) writes that a single approach cannot always be carried out but it takes human ideas and criticism to evaluate things in a different way or a constructivist approach which uses qualitative methods. This leads to the idea that the paradigms can overlap and a mixed methodology applied for instance, applying a set of criteria or a system to locate information but critical evaluation of methods and results in a descriptive analysis. Realism views that one reality exists that can be measured and cannot change; while relativism means that there can be multiple truths and the perceptions of truth can change over time. Applying this to endodontics would mean that whilst there is a need for a positivist approach to show transparency, finding the answers is never easy and relativism may help acquire further knowledge and ask questions in a different way. As there can be considerable overlap in these paradigms with none being held as superior, in some situations they could be combined in the research methodology, making it is difficult to categorise the paradigm (Gordon, 2016). The paradigm in this case could be categorised as post-positivism with elements of constructivism in accepting that there may be more than one truth (Gordon, 2016).

It is seen that in vitro studies have good internal validity but lack external validity (Krithikadatta, 2012; Linares-Espinós et al., 2018). Internal validity can give data on whether the procedure works or whether the results of the study are accurate for the conditions of the study but external validity gives information on whether this is useful to the population (Krithikadatta, 2012; Linares-Espinós et al, 2018). The cyclic fatigue studies carried out are mostly experimental or in vitro studies. Although in vitro studies are considered a low level of evidence (see appendix C), the higher levels of evidence like randomised controlled trials are not available or practical as they would be considered unethical (Krithikadatta, 2012; Bergenholtz & Kvist, 2014; Haapasalo, 2016). Using extracted teeth would be the preferable alternative but handling of human teeth is subject to ethical approval and has other problems such as difficulty in standardisation of testing conditions (Krithikadatta, 2012).

Experimental studies, even though considered a low level of evidence, can provide the necessary raw material for higher levels of studies (Haapasalo, 2016). Haapasalo (2016) mentions that although in vitro studies are considered a low level of evidence in the levels of evidence, it should not be considered weak or unreliable, especially when other levels of evidence are unavailable but the strength for drawing conclusions for long term results needs to be interpreted with caution. The pyramid on the levels of evidence (see Appendix C) does have a positivist view but applying a critical need whether certain studies are ethically necessary and using the next best available data, entertains a relativism approach.

Whilst contacting the authors of studies for further clarification or dealing with missing data is considered highly desirable (Delgado-Rodríguez & Sillero-Arena, 2018), a recent study highlighted several problems from a lack of procedure on how contact should be made or methods to report findings, to a lack of response from the authors of primary studies (Reynders, Ladu & Di Girolamo, 2017). The authors contacted can give false positive responses depending on the way contact is made (Higgins & Green, 2011), so it was decided not to contact any of the authors of primary studies.

It was decided to exclude studies that are not in English, as it can be time consuming to translate and increase the burden of work for a single reviewer. Juni, Holensteien, Sterne, Bartlett and Egger (2002) observed that non-English studies tended to observe more positive findings in the results, which could be due to small sample sizes and whilst effort to include all studies is desirable, costs and resources to translate studies make it practically difficult, concluding that excluding non-English studies made little difference to the results. Espinós-Linares et al. (2018) also suggested that it would hardly make a difference to the findings. Most endodontic studies are translated to English, if not published initially in English, so the risk of language bias would be very small.

Grey literature is usually literature that has not been formally published in books or journals, can be difficult to source on the topic but effort will be made to find any (Higgins & Green, 2011; Delgado-Rodríguez & Sillero-Arena, 2018). Literature located could be in a different language, for example, DissOnline is a German dissertation website (Higgins & Green, 2011). However, just including published studies can introduce bias, as unpublished studies may be studies without significant findings and for this reason have not been published (Higgins & Green, 2011). Searching grey literature databases may have studies which are not representative of all unpublished data on the topic which may bring about an additional bias (Higgins & Green, 2011).

An initial search and background review of the literature available was carried out with the following questions:

- Which files can be described as being in the martensitic state?
- What are the potential benefits of using martensitic phase files?
- Are there any systematic reviews of cyclic fatigue in martensitic phase files?
- What are the types of studies available?
- Identifying factors which can affect cyclic fatigue resistance in martensitic phase files?
- Has a systematic review been carried out before? Is there a need for a systematic review? (Higgins & Green, 2011; Delgado-Rodríguez & Sillero-Arenas, 2018).

The initial searches using Wiley and Science Direct databases revealed that there was no systematic review of cyclic fatigue resistance in martensitic NiTi rotary files. It also identified a variety of files which did possess a small amount of the martensitic phase but for purposes of this review it was decided to focus on files where the majority of the state of NiTi alloy at intracanal temperatures is thought to be martensitic. A review by Zupanc et al. (2018) and Gavini et al. (2018) identify the martensitic phase files, which will help to formulate the list of files to be included in the review. Manufacturers of these files and various studies have reported an increased cyclic fatigue resistance (Pirani et al., 2016; Kaval et al., 2016). The review identified factors affecting cyclic fatigue resistance and efforts shall be made to include and search for the effects of these various factors on the martensitic files included in the review.

3.2. Stages of the Research

3.2.1. Framing the title for the review

The criteria will be established using a Problem, Intervention, Comparison, Outcome and Study design (PICOS) strategy (Liberati et al., 2009; Higgins & Green, 2011). This will help structure the questions to ask and review. Linares-Espinós el al. (2018) stated that a well-formulated title is needed, which is created using PICOS, which stands for the population under study (population/ problem), the intervention being studied (intervention/ exposure), the comparison of the intervention (comparator), outcomes or results (outcome) and study type selected (study design).

The problem: The separation or breakage of NiTi rotary files, which can occur during cleaning and shaping of the root canal. If the file could not be retrieved this could lead to the incomplete cleaning of the canal space beyond the fractured instrument.

The intervention: Increasing the martensitic phase of a NiTi rotary file by thermal processing or cold working during the manufacture of the file. Variations in taper, design, surface treatments and movement of the files can affect the fatigue resistance.

The comparator: Variations in martensitic file content and files which have a mixture of small amounts of other phases like austenitic and R-phase and the effect of temperature.

The outcome: The effect on the cyclic fatigue resistance and preventing instrument separation by identification of factors which can influence the cyclic fatigue resistance.

The study design: Studies found are in vitro studies, so in vitro studies examining the cyclic fatigue resistance will be included.

From the PICOS, a review title was formulated “Cyclic fatigue resistance of nickel titanium rotary files in the martensitic state: A systematic review ”.

Table 3.1. PICOS table (The author’s own work, 2019).

Study ID		
PICO	Inclusion variables	Response
Review question	Cyclic fatigue resistance of nickel titanium rotary files in the martensitic state: A Systematic Review.	
Population / Patient / Problem	Files described as martensitic such as Hyflex EDM, ProTaper Gold, WaveOne Gold, Reciproc blue, Vortex Blue. Studies using intracanal temperature at or near body temperature. Instrument Separation/ File fracture.	
Intervention/ Exposure	Variations in martensitic phase Variations in the instrument’s size and taper. Variations in the movement of the file. Variation in surface treatment. Variations in testing methods .	
Comparator	Different types of martensitic files. The effect of other factors. The effect of temperature. Comparison to austenitic files.	
Outcome	Increased cyclic fatigue resistance. Prevention of instrument separation. Efficiency in endodontic treatment. Clinical treatment planning. Future areas for research.	
Setting	Preclinical	
Study design	IN VITRO studies No higher levels of evidence available	

3.2.2. Formulating inclusion and exclusion criteria

The PICOS (Table 3.1) can be used to help develop a PICO concept map (University of Leeds, 2019). This concept map can identify words and terms that can be used in developing a search strategy (table 3.2). From table 3.2, it can be seen that there are various possibilities for search combinations and similar words can be identified and charted. The reviewer needs to identify martensitic phase files available and formulate a list, as there is little in the literature identifying these files and using the term “martensite” or “martensitic files” would not give any results in the preliminary search.

Table 3.2. PICOS concept map (Authors own work, 2019).

PICO heading	Stands for	Search term possibilities
P	Population Patient Problem	Martensitic files /names of martensitic files Separation/ file fracture CM files Gold files Blue files Cyclic fatigue resistance / Flexural fatigue
I	Intervention Exposure	Martensitic phase Temperature Heat treatments Surface treatments Cyclic fatigue testing conditions
C	Comparator	Martensitic files /CM files Gold Files Blue files Temperature Movement of file Reciprocation / rotation Taper / design of the file
O	Outcome	Prevent separation Sequence of instrument Single file system Hybrid file systems Lowering Temperature

Gavini et al. (2018) and Zupanc et al. (2018) described the martensitic files as having a mixture of austenite and martensite phases forming a hybrid phase and that increasing the percentage of martensitic phases favours increased cyclic fatigue resistance. Zupanc et al. (2018) divides the file systems into conventional (austenitic) and martensitic types, including controlled memory NiTi alloy, gold NiTi alloy, blue NiTi alloy, EDM alloy and MaxWire^{TM} (Table 3.3).

Table 3.3. Files showing martensitic phases. Adapted from “New thermomechanically treated NiTi alloys - a review,” by Zupanc et al., 2018, *International Endodontic Journal*, 5 (10), p. 1091.

Alloy	Phase composition at intracanal temperature	NiTi file system
CM wire	Austenitic with martensite and R-phase	Hyflex CM, Typhoon Infinite flex Niti files, V-Taper 2H, Prodesign–R, Prodesign Logic, Kontrolflex, Sequence, 2shape, One Curve TRUShape?
CM but produced by EDM	Martensite and R-phase	Hyflex EDM
Gold heat–treated	Austenitic with martensite and R-phase	ProTaper Gold WaveOne Gold
Blue heat-treated	Austenitic, martensite and R-phase	P Vortex Blue Reciproc Blue
Max Wire	Initially martensitic at 20 °C and becomes austenitic above 35 °C	XP-Endoshaper

The CM wire is controlled memory NiTi which has some martensitic phases (De Menezes, Batista, Lira & De Melo Monteiro, 2017). In an effort to further clarify the file systems which are martensitic, the author decided to look at transition temperatures for these files as it is considered that if the A_s is above body temperature, then no austenite phases will be present at intracanal temperature (Table 3.4). CM files are a mixture of austenite and martensite with small amounts of R-phase, with Hyflex CM having an A_f of 32 - 37 °C. The A_s of Hyflex EDM is 42 °C and consists of martensite and R-phase; this R-phase has titanium nitrate precipitates. Vortex Blue has an A_f of 38.5 °C and M_s of 31 °C, so it would be a mixture of phases at intracanal temperature, with both gold and blue treatments having more martensite phases than present in M-wire. M-wire has an A_f of 43 - 50 °C and contains the austenitic phase with small amounts of martensite and R-phase at room temperature, resulting in stiffer files which maintain a superelastic state like Protaper Next^{TM} and Profile Vortex. These are excluded from the review as they contain a very small amount of R-phase and behave in a superelastic way.

Gavini et al. (2018) and Zupanc et al. (2018) mentioned that the XP-EndoShaper file which is made from Maxwire is martensitic when inserted in the canal but changes to an austenitic state in the canal; as it starts to work in the martensitic state at insertion into the canal, the XP-Endoshaper is included in the review. Some newer files had insufficient details on the dominant phase of the metal and presumably will have some martensitic phases present such as 2shape™, OneCurve™ and Sequence™ (Gavini et al., 2018). Another way to define martensitic files is to look at temperatures where martensite starts to form M_s and when it finishes formation or M_f. The technique to measure transition temperatures uses differential scanning calorimetry or DSC. This method measures the difference in heat energy uptake, between a sample compared to a known reference sample, during a regulated temperature change; as the energy uptake of the reference is known, any difference in energy taken up by the unknown sample can be compared and correlated to its properties (Durowoju, Bhandal, Hu, Carpick & Kirkitadze, 2017). DSC can vary between used and new files, different parts of the same file, which can be due to work hardening and changes in the structure which occur during use, like the formation of stress induced martensite. Brantley, Svec, Iijima, Powers and Grentzer (2002) demonstrated variation in the transformation temperatures from different parts of the Profile™ and Quantec™ files, claiming this was due to variations in processing or subsequent clinical use.

There are also gaps in the literature available regarding transition temperatures for R-phases on ProTaper Gold, which has an estimated M_s of 40 °C and M_f of 30 °C (Hieawy et al., 2015). Hyflex EDM has R_s of 46 °C, R_f of 36 °C, A_s of 37 °C and A_f of 53 °C but M_s of 48 °C meaning it would be operating in R-phase with some martensitic phases present (Iacono et al., 2017; Pedulla et al., 2019). WaveOne Gold has R_s of 44 °C and R_f of 25 °C which means it would be working in R-phase (Pedulla et al., 2019); whilst Reciproc Blue has R_s of 46 °C, R_f of 27 °C and A_s 33 °C having R-phase and a small percentage of austenitic phases (Almeida et al., 2019). As there is some variation seen in the temperatures reported by different authors, it is difficult to use to this method alone to create a list of martensitic files.

Table 3.4. Transition temperatures in files. yellow highlights are information obtained from studies included in the systematic review which has been added (Authors own work, 2019).

Files	M_s (°C)	M_f (°C)	R_s (°C)	R_f (°C)	A_s (°C)	A_f (°C)	Reference	Dominant phase 31-36 °C
Hyflex CM	-18.3 -5	-42.34 -32.3	29.35	17.44	11.81 21.5	39.75 50 43.5	Shim et al., 2017 Gu et al. , 2017 de Vasconcelos et al.,2016	Austenitic mostly
Reciproc	44.85	-13.44			-1.87	58.1	Shim et al. 2017	Austenite
K3	3.84	-47.83			-39.6	6.53	Shim et al. 2017	Austenitic
Twisted file	43.54	-25.39	-35.3	12.04	12.04	51.74	Shim et al. 2017 Gu et al.,2017	Austenitic
Vtaper 2H						33.25 44.95	Chang et al., 2016 Gu et al.,2017	Austenitic ?
Profile Vortex(new)	47.4	16.1			28.1	53.1	Shen et al., 2015	Austenitic
WaveOne						50.38	Gu et al., 2017	Austenitic
K3XF						24.8	Zhou et al.,2013	Austenitic
Typhoon CM	26.27	-27.26			24.42	55.09 55	Shen et al., 2011 Zhou et al.,2013	Austenitic
One Shape						10-18	Staffoli et al., 2018	Austenitic
2Shape						17	Kaloustian et al.,2019	Austenitic
TRUShape	30	20			22	31	De Vasconcelos et al.,2016	Austenitic
One Curve						40-50	Staffoli et al., 2018	martensitic ?
Hyflex EDM	48-50 -17.1?	-26 -41.22	46 46.08	36 35.59	42-43 37.25	51-54 53.56	Iacono et al., 2017 Arias et al. 2018 Pedulla et al., 2019.	R-phase. Check R_s and R_f temp. R phase and martensite
ProTaper Gold	40? From graph	30? cooling graph			About 40	50.1	Hieawy et al., 2015	martensitic R_s R_f needed
WaveOne Gold	11.05	28.87	44.62	25.01	35.08	40-60 49.31	Aoun et al., 2017 Pedulla et al., 2019	R phase ?need DSC R phase
Reciproc Blue			46.8	27.5	26.9-28.7 33.8	30.73 34.8-36 51	Inan et al., 2019 Plotino et al., 2018 Almeida et al., 2019	Austenite Martensitic R phase, austenite
Vortex Blue (new) (Used)	31.1 28.9	22.3 21.6	33.61	30.89	31.6 30.1 30.81	38.5 36.2 33.71	Shen et al.,2015. Zupanc et al.,2018 De Vasconcelos et al., 2016 Arias et al., 2018	Austenitic r phase R phase at intracanal
XP Endo Shaper						35	Adiguzel et al., 2018	Martensite? Need DSC

The shape memory property of martensitic phase alloys allows the practitioner to pre-curve the instrument (Table 3.5). This property is due to shape memory at room temperature and is seen in Hyflex EDM, Protaper Gold, WaveOne Gold, Reciproc Blue^{TM}, Vortex Blue, One Curve^{TM} ,Kontrolflex^{TM} and XP-Endoshaper. This property, along with transition temperatures is used to formulate a list of martensitic files.

Table 3.5. Files which show shape memory effect and can be pre-curved. (Author's own work, 2019).

Pre-curved files or files showing shape memory	Reference
Vortex Blue	Elnaghy & Elsaka, 2018.
Reciproc blue	Gavini et al., 2018.
Wave One Gold	Van Der Vyver & Vorster, 2015.
Protaper Gold	Publicity materials (Dentsply, 2015).
Hyflex EDM	Publicity materials (Coltene UK, 2018).
One Curve	Elnaghy & Elsaka, 2018.
KontrolFlex	Publicity materials (Brasseler USA, 2019).
XP Endo Shaper	Elnaghy & Elsaka, 2018.

The inclusion criteria (Table 3.6) include studies which are in English, on file systems specified in table 3.5 and includes in vitro tests on cyclic fatigue using temperature between 31 – 37 °C. Various factors which can affect cyclic fatigue resistance will be reviewed and included in the criteria such as the effect of temperature, the presence of irrigants, rotational speed, instrument design and kinematics or movement of the files. Articles from the last five years are included, so that the data obtained is relevant and current.

Table 3.6. Inclusion Criteria for Studies (Author's own work, 2019).

Studies are in English.
Studies are on cyclic fatigue resistance in the specified files. Files which may be pre-curved and show shape memory properties mentioned in Table 3.5.
Studies are in vitro studies.
Studies that are identifying various factors which can influence cyclic fatigue in the specified files like the effect of irrigants, temperature, rotational speed and kinematics.
Studies conducted at temperatures within 31 – 37 °C.
Dates from 2014 onwards to include the most recent work in the last 5 years.

Table 3.7. Exclusion Criteria (Author's own work, 2019).

Case reports.
File systems that are not mentioned in Table 3.5 as pre-curved files.
Duplicate articles.
Review studies or studies already reviewed in the literature review.
Studies that are not in English.

The exclusion criteria excluded case reports or expert opinions as these are considered a low level of evidence (see Appendix C). Torsion studies are excluded unless reviewed as a factor affecting cyclic fatigue resistance. Studies not in English and file systems not in table 3.5 are excluded. Reviews or studies included in the initial literature review are excluded from the systematic review to avoid duplication of material already identified.

3.3. Search Strategy:

The systematic review is conducted by a single reviewer. The searches would be carried out using the following databases or organised collections of data (Centre for reviews & Dissemination [CRD], 2009; Higgins & Green, 2011).

- Science Direct
- Wiley Online Library
- PubMed/ Medline
- Google Scholar

The databases included are commonly used in the medical world which would give a comprehensive list of studies but may give rise to many duplicate studies being identified (Higgins & Green, 2011). Embase is another database recommended but as there is an overlap in studies found between the different databases, it is assumed that omitting this database would not impact the results (Higgins & Green, 2011). Scopus which is used later in the citation searches includes PubMed and Embase (Delgado-Rodríguez & Sillero-Arena, 2018). The Cochrane database has randomised clinical trials (Higgins & Green, 2011) but as none can be carried out for a separated instrument due to ethical reasons, it was found not to have any relevant studies in this field. The reviewer will search for any ongoing or completed reviews on PROSPERO which is a database on current systematic reviews being carried out (Higgins & Green, 2011). The reviewer will perform a hand search of the reference list of eligible articles to find more studies which will then be screened. The abstracts and full texts will be screened applying inclusion and exclusion criteria. The reviewer will perform a citation search and include any full text articles that meet the inclusion criteria.

The details on search terms used and search strategy will be listed separately for each database searched and adjusted according to each database (Higgins & Green, 2011). The use of keywords with the appropriate Boolean operators like “AND” and “OR” which are typed together on the Science Direct database in the “title / abstract / key word” field leaving all other columns blank (table 3.8). The “years” field is filled with a range from 2014 - 2019. A need to be more specific and efficient was identified to create an easier reproducible search method so the search terms were adjusted accordingly after initial searches (Higgins & Green, 2011; Baird, 2018). Using the “find articles with these terms” field may increase the sensitivity or the comprehensive nature of the review but this may be more time consuming as a lot of irrelevant literature was found (Higgins & Green, 2011).

Table 3.8. Key words for searching the Science Direct database (The author’s own work,19/03/2019).

Search words in “title/abstract /keywords”	Number of articles retrieved
Cyclic fatigue AND Hyflex Cyclic fatigue AND Vortex Cyclic fatigue AND Gold Cyclic fatigue AND Blue	20 (16 excluded, 4 included) 26 (23 excluded, 3 included) 20 (15 excluded, 5 included) 20 (19 excluded, 1 included)
Cyclic fatigue resistance AND temperature AND files	14 (all excluded, mostly duplicates)
Cyclic fatigue AND XP Cyclic fatigue AND Typhoon Cyclic fatigue resistance AND 2 shape Cyclic fatigue resistance AND One Curve files Cyclic fatigue resistance AND Sequence Cyclic fatigue resistance AND Kontrolflex Cyclic fatigue resistance AND Prodesign Cyclic fatigue resistance AND V Taper	3 (2 excluded, 1 included) 3 (all excluded) 1 (excluded) 14 (13 excluded, 1 included) 5 (excluded) 0 1 (excluded) 1 (excluded)

Search words in “find articles with these terms”	Number of articles retrieved
Cyclic Fatigue resistance AND intracanal temperature AND heat treated file	35 articles (all excluded with reasons)
Cyclic Fatigue resistance AND martensite AND intracanal temperature	23 articles (all excluded)
Cyclic Fatigue resistance AND martensite AND reciprocation AND files	29 articles (all excluded)

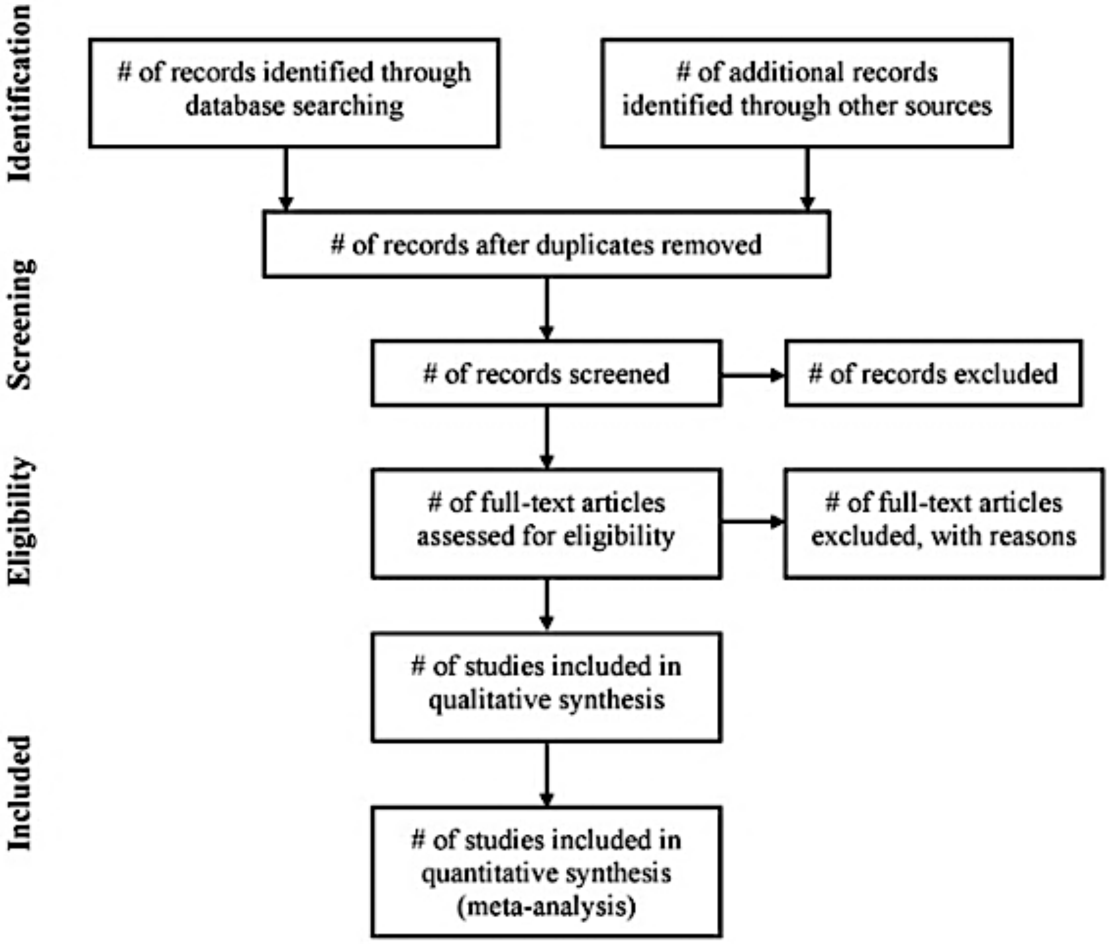
Snowballing and Citation searches:

Snowballing which is evaluating the reference list of included studies and reverse snowballing which is evaluating the literature that cites the included studies will be carried out (Baird, 2018). Reverse snowballing is done using a citation search database such as Scopus and Web of Science (Moher et al., 2008; Higgins & Green, 2011). Results from these searches are added to the studies so that abstracts and then full texts can be screened.

3.4. Data extraction and management

The Preferred Reporting of Items in a Systematic review and Meta-Analysis (PRISMA) flowchart (Table 3.9) is a four phase diagram that will provide a means to show the flow of information through various phases of the systematic review (Moher, Liberati, Tetzlaff & Altman, 2009). There is also a 27-point checklist (see Appendix F) which helps provide guidance for a systematic review.

Table 3.9. PRISMA flowchart showing the flow of information during phases of the review. From "Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement," by Moher et al., 2009, *Journal of Clinical Epidemiology*, 62, p. 1009.



The records identified will be screened first by titles to exclude irrelevant data (Higgins & Green, 2011). The reviewer will then apply inclusion and exclusion criteria (Table 3.6 & 3.7). Studies are selected by screening the abstracts and titles, with studies failing to meet the criteria excluded; some may be marked as uncertain and are then subjected to a full text screen after which the study should either be included or excluded (CRD, 2009;

Higgins & Green, 2011; Linares-Espinós et al., 2018). Duplicates will also be identified and removed during both screenings; with reasons for exclusion being clearly documented (CRD, 2009). The included articles will then be checked through citation search and reference lists for these studies searched for any studies that have not been identified in earlier searches (Higgins & Green, 2011). The studies which have been included are then presented in a table to create a study ID with brief details of each study and this ID is used in the data extraction forms (Table 3.10).

Table 3.10. The Study ID form (The author's own work, 2019).

Study ID	Year	Authors	Title

A data extraction form is used to present studies includes headings like study ID, temperature, canal curvature, the radius of curvature, canal material, sample size, the name of files, file size, taper, torque, movement, speed of files and outcomes/ results (Table 3.11). The study ID will be used for a PICO data extraction form (Table 3.12).

T**able 3.11. The Data Extraction form** (The author's own work, 2019).

ID	T/°C	CC &R	Canal	SS	NiTi file	FS	Taper	Speed &Torque	Results (NCF)
KEY. ID: Study ID, T: Temperature, CC: canal curvature, R: the radius of curvature of the canal, SS: Sample size, FS: file size, NCF: the number of cycles to fracture.									

Table 3.12 .The Sample PICO data extraction form (The author's own work, 2019).

Study ID	Population	Intervention	Comparator	Outcome

3.5. Data Analysis

A single reviewer will analyse the data and provide a descriptive analysis. It is important that the review is carried out in a systematic way, that is reproducible and has to show a greater transparency as it is carried out by a single reviewer (Linares-Espinós et al., 2018). Higgins and Green (2011) describe the quantitative statistical analysis or meta-analysis as a way to combine the results from two or more studies by statistics. However, as there is diversity or heterogeneity in the methods of testing from custom fit metal canals, various sample sizes, various tapers and sizes of files, various methods of recording file breakage, various curvatures, problems with standardisation of in vitro testing, it can be considered that a meta-analysis would not be suitable. A meta-analyses or statistical analysis can only be carried out if studies have good similarity or validity as if there are errors in the study designs then positive findings will need to be interpreted with caution so a narrative synthesis is carried out and no study is inappropriately given credibility over another (Liberati et al., 2009; Higgins & Green, 2011).

3.6. Quality Assessment of the primary studies

A review of quality of studies included in the systematic review can be carried out using the checklist for cohort studies from the Joanna Briggs Institute (Table 3.13). The checklist has questions regarding the random allocation of files to groups, the operator being concealed from file allocation, the outcome assessors blind to treatment or group assignment, outcomes measured in the same way and reliable way for all groups, whether groups were treated identically and if the appropriate statistical analysis is used.

Table 3.13. The Quality of the primary studies using the checklist for cohort studies from the Joanna Briggs Institute. From “Critical appraisal checklist for cohort studies. JBI reviewer’s manual,” by Joanna Briggs Institute, 2019, (https://wiki.joannabriggs.org/display/MANUAL/Appendix+7.1++Critical+appraisal+checklist+for+cohort+studies).

Study ID	1	2
JB1. Is the assignment of participants to treatment groups random?		
JB2. Were participants blinded to allocation to treatment groups ?		
JB3. Was allocation to treatment groups concealed from the allocator?		
JB4. Were outcome assessors blind to treatment assignment?		
JB5. Were treatment groups treated identically other than the intervention of interest?		
JB6. Is follow up complete and if not, were differences between groups in terms of the follow up adequately described and analysed?		
JB7. Were participants treated identically in the groups to which they were randomized?		
JB8. Were outcomes measured in the same way for treatment groups?		
JB9. Were outcomes measured in a reliable way?		
JB10. Was the appropriate statistical analysis used?		
Key Input data: Yes/ no / NA(not applicable)/ not-stated		

The risk of error in the primary studies needs to be identified and assessed. Bias is defined as any process at any part of the study that can cause the results to change from real values (Linares-Espinós et al., 2018). It is systematic deviation in the form of results or conclusions that can occur in either a positive or negative direction, leading to an underestimation or overestimation of the effect (Higgins & Green, 2011). A bias occurs in a systematic way, which if the experiments are repeated, it gets reproduced repeatedly giving similar results; rather than random error or imprecision which occurs randomly and may give different results (Higgins & Green, 2011). Eliminating bias or identifying sources of bias can help interpret its effects on the results of the study and identify the value of information from a study.

Higgins and Green (2011) and Linares-Espinós et al. (2018) categorize bias as selection, detection, performance, attrition, reporting and other biases (See Appendix E). Selection bias is described as errors during allocation of samples to groups, detection bias as errors during detecting outcomes, performance bias as errors in exposure of samples to other factors, attrition bias as the loss of samples, reporting bias as failure or selective reporting on outcomes or incomplete data and a category for other errors which are specific to the type of study. The allocation sequence is the chance of a sample being allocated to a particular group and random selection maintains the chance that a sample could be in any group.

Blinding or masking means that the researcher should not know which sample is assigned to which group, or which group is being assessed for an outcome but this would need more than one researcher (Krithikadatta, Gopikrishna & Datta, 2014). Standardisation of in vitro studies can be more difficult but is needed, from sample sizes to checklists on limitations (Chander, 2016). Krithikadatta et al. (2014) stated the need for guidelines to promote greater transparency in reporting of in vitro studies. The areas highlighted were sample size calculation, the meaningful difference between the groups studied, allocation sequence, randomisation, blinding and statistical analysis used in studies.

The method of sample size calculation is often not mentioned in studies (Higgins & Green, 2011; Krithikadatta et al., 2014). Sample sizes can be small, which creates chances of a positive finding being regarded as true, whilst a large sample size can make an insignificant finding seem significant (Faber & Fonseca, 2014). The researcher decides what a meaningful difference is, so if a large value is chosen this could mean a smaller sample size is used to get this result or vice versa. In the author's opinion, cyclic fatigue tests can have the files randomly allocated in groups to create blinding but this may increase the risk of errors if the files are not labelled accurately by another method. A selection bias could be reduced by having a different operator randomly assigning files to groups and making the files difficult to be identified by the operator. A second operator performs the test and a third operator analyses the results. In the studies identified in the literature review, it is possible that the same person is carrying out all stages, knows the files involved, operates the stopwatch and reports the outcomes knowing the groups or files involved so no blinding or randomisation can be identified. Statistical analysis can give different results if the wrong statistics are applied so the results of the analysis should be interpreted with care (Krithikadatta et al., 2014).

3.7. Assessment of Bias in the systematic review.

Higgins and Green (2011) mention various errors can occur during the different stages of the systematic review. A publication bias occurs if only published studies are included; a language bias if a single language is chosen; a time lag when certain studies with insignificant results can be delayed by years so the review can have more significant results then actually present if all studies were available. The time lag and publication bias can be reduced by trying to find all available grey literature. Funding can cause a conflict of interests if the source of funds needs a particular outcome; duplicates if undetected can give more significance to findings. There can be errors in the way outcomes are reported or abstracts can be eliminated early without screening the content properly. Citation bias can occur when screening reference lists as authors may reference articles confirming their point of view and location bias can occur if using particular electronic databases or journals. Table 3.14 shows the categories of the risk of bias in the review process.

Table 3.14. Bias in the Systematic review. Adapted from "Reporting Biases," Cochrane Handbook, by Higgins and Green, 2011, (https://methods.cochrane.org/bias/reporting-biases).

Type of Bias	Risk	Comments
Publication		
Language		
Time lag		
Funding		
Citation		
Location		
Search		
Duplicate publication		
Abstract to full text		
Outcome reporting Bias		

3.8. Ethical considerations

Plagiarism is using another person's work or ideas without acknowledgement; but manipulation of data to increase the results or reduce the significance can also occur (Guraya, London and Guraya, 2014). Wager and Wiffen (2011) stated that fraudulent data, incomplete data and plagiarism in the original studies can be missed and a systematic review can give incorrect data a stronger level of support; this needs to be identified and either authors should be contacted for clarification or these studies excluded. If there are too many studies by the same author, this can also result in errors in the data being magnified, so there is a need to highlight this if it occurs. There are no ethical guidelines on systematic reviews so there is a need to establish guidelines.

In examining the problems of cyclic fatigue testing, the use of human tissue such as teeth are under regulations of the Human Tissue Act (2004) which requires the donor's consent and tightly regulates facilities for storage of tissue samples (Human tissue authority, 2017). As other testing methods are available which provide higher standardisation it is unlikely that cyclic fatigue tests on human teeth or a clinical trial would gain approval by ethical boards (Bergenholtz & Kvist, 2014). A pilot study on human tooth tissue would need to be carried out to identify the need to use tooth tissue but this would need ethical approval. In the UK, most extracted teeth are incinerated but all extracted teeth could be donated to a storage bank instead for use in future research projects, with researchers taking samples from this bank and not directly from any patient under their care. A recent study on extracted teeth by Bueno et al. (2017) reported a very low incidence of fracture of reused reciprocating files WaveOne™ and Reciproc™, with all separation occurring in the canals of mandibular molars. Ex-vivo studies such as these may provide a higher level of evidence than tests using current cyclic fatigue testing methods (Krithikadatta, 2012; Bergenholtz & Kvist, 2014; Haapasalo, 2016).

Results

4.1. Description of the studies

4.1.1. Results of the search

The databases searched are Science Direct, PubMed, Wiley and Google Scholar (Table 4.1). Science Direct database obtained 215 articles from which 15 were included.

Table 4.1. Searches on Science Direct, PubMed, Wiley and Google Scholar (The author's own work, 2019)

Database: Science Direct. Total articles found 215. Included 15.	
Search words in "title/abstract /keywords"	Number of articles retrieved
Cyclic fatigue AND Hyflex Cyclic fatigue AND Vortex Cyclic fatigue AND Gold Cyclic fatigue AND Blue	20 (16 excluded, 4 included) 26 (23 excluded, 3 included) 20 (15 excluded, 5 included) 20 (19 excluded, 1 included)
Cyclic fatigue resistance AND temperature AND files	14 (all excluded as mostly duplicates)
Cyclic fatigue AND XP Cyclic fatigue AND Typhoon Cyclic fatigue resistance AND 2 shape Cyclic fatigue resistance AND One Curve files Cyclic fatigue resistance AND Sequence Cyclic fatigue resistance AND Kontrolflex Cyclic fatigue resistance AND Prodesign Cyclic fatigue resistance AND V Taper	3 (2 excluded, 1 included) 3 (all excluded) 1 (excluded) 14 (13 excluded,1 included) 5 (all excluded) 0 1 (excluded) 1 (excluded)

Search words in "find articles with these terms"	Number of articles retrieved
Cyclic Fatigue resistance AND intracanal temperature AND heat treated file	35 articles (all excluded with reasons)
Cyclic Fatigue resistance AND martensite AND intracanal temperature	23 articles (all excluded)
Cyclic Fatigue resistance AND martensite AND reciprocation AND files	29 articles (all excluded)

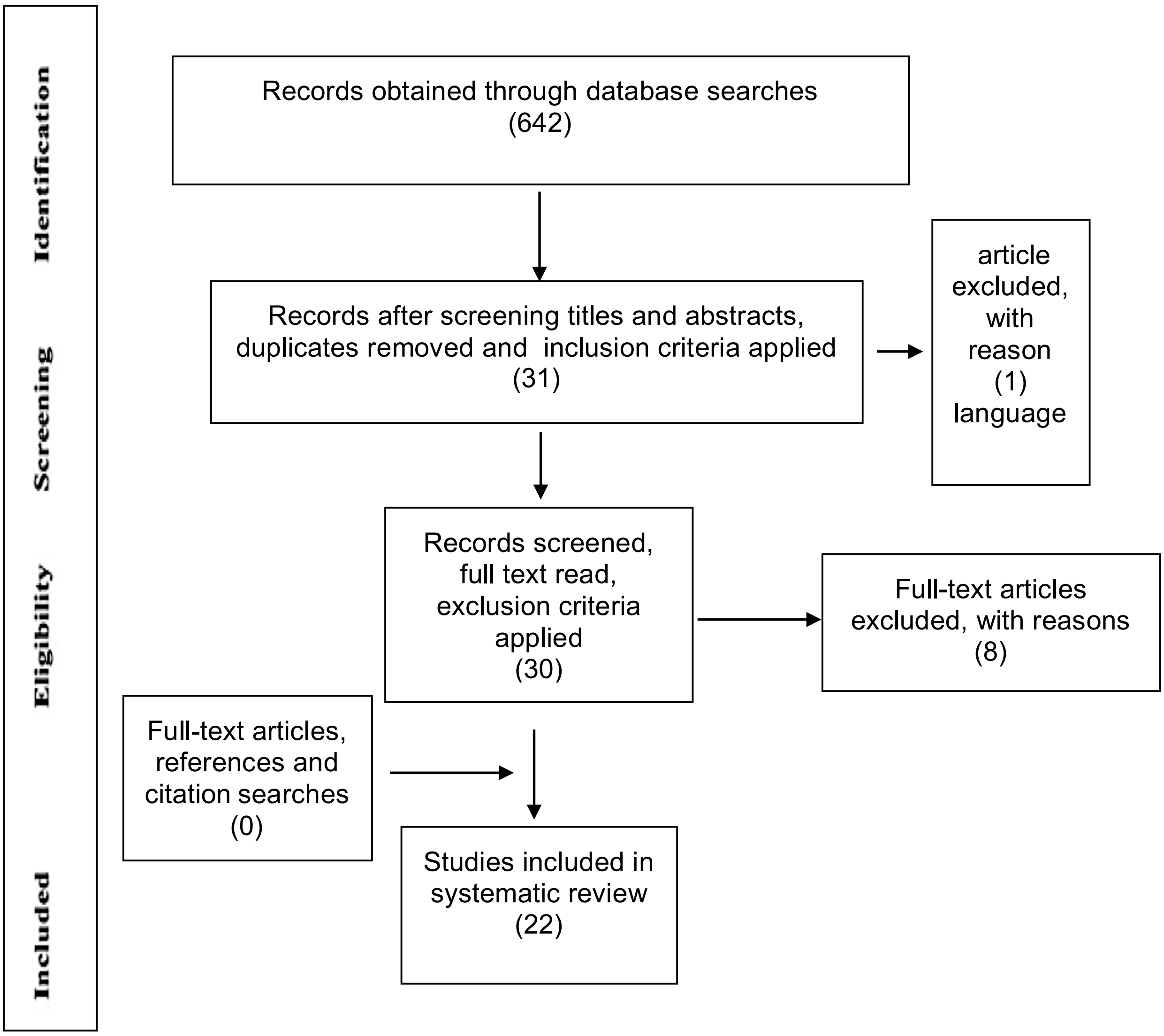
Database: Pub Med. Total articles found 87. Included 7.		
Search	MeSH	Number of articles
#1	Cyclic fatigue AND temperature AND files	39 (35 excluded, 4 included)
#2	Cyclic fatigue AND temperature AND martensitic	6 (5 excluded, 1 included)
#3	Martensitic files AND cyclic fatigue AND temperature	2 (excluded)
#4	CM files AND cyclic fatigue AND temperature	10 (all excluded)
#5	Blue files AND cyclic fatigue AND temperature	8 (all excluded)
#6	gold files AND cyclic fatigue AND temperature	7 (all excluded)
#7	Hyflex AND cyclic fatigue AND temperature	15 (13 excluded, 2 included)

Database: Wiley. Date range: 2010-2019. Articles retrieved 73. Included 2.		
In text	Terms used	Number of articles
Titles Titles anywhere	Files AND Cyclic fatigue AND Temperature	4 (all excluded with reasons)
Anywhere Title anywhere	Hyflex AND Cyclic fatigue AND temperature	7 (all excluded with reasons)
Anywhere Title anywhere	CM files AND Cyclic fatigue AND Temperature	8 (7 excluded, 1 included) Elnaghy and Elsaka 2016.
Anywhere Title anywhere	gold files AND Cyclic fatigue AND Temperature	6 (5 excluded, 1 included) Keles et al., 2019.
Anywhere Title anywhere	blue files AND Cyclic fatigue AND Temperature	4 (all excluded with reasons)
Anywhere Title anywhere	EDM files AND Cyclic fatigue AND Temperature	2 (all excluded with reasons)
Title Anywhere Anywhere Anywhere	Cyclic fatigue AND Martensitic AND Temperature AND Files	4 (all excluded with reasons 2 irrelevant and 2 no mention or not at body temp)
Anywhere Anywhere Anywhere Anywhere anywhere	Cyclic fatigue AND Martensitic AND Temperature AND Files AND Endodont*	38 (all excluded with reasons)

Database: Google scholar. Date range: none . Total articles found 267. Included 7.	
Search terms	Number of articles retrieved
Cyclic fatigue temperature	60
Cyclic fatigue resistance temperature	18 (16 excluded, 2 included)
Cyclic fatigue resistance Hyflex	10 (9 excluded, 1 included)
Cyclic fatigue resistance Gold	34 (all excluded)
Cyclic fatigue resistance Blue	13 (all excluded)
Cyclic fatigue XP	4 (3 excluded, 1 included)
Cyclic fatigue CM	6 (5 excluded, 1 included)
Cyclic fatigue resistance Kontrolflex	0 (none)
Cyclic fatigue Typhoon	0 (none)
Cyclic fatigue AND gold	28 (27 excluded, 1 included)
Cyclic fatigue AND blue	20 (19 excluded, 1 included)
Cyclic fatigue AND EDM	9 (all excluded)
Cyclic fatigue AND Endosequence	6 (all excluded)
Cyclic fatigue Prodesign	1 (excluded)
Cyclic fatigue AND V taper	2 (excluded)
Cyclic fatigue AND 2shape	3 (all excluded)
Cyclic fatigue AND one curve	3 (all excluded)
Cyclic fatigue reciprocation	7 (all excluded)
	Total:267 Included :7

The results from Wiley obtained 73 articles, from which 2 were included. The searches on the PubMed database obtained 87 articles, from which 7 were included and Google Scholar obtained 267 articles, from which 7 were included. The PRISMA flowchart (Table 4.2.) shows the total records obtained at 642. After screening titles and abstracts, there were 31, 1 was excluded, resulting in 30. These 30 were subjected to full text screening applying inclusion and exclusion criteria, 8 articles were excluded with reasons. The remaining 22 articles were subjected to reference list searches and citation searches but no additional records were identified.

Table 4.2. PRISMA flowchart to show flow and gathering of data in different stages of the review. Adapted from “Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement,” by Moher et al., 2009, *Journal of Clinical Epidemiology*, 62, p. 1009.



4.1.2. Included studies

Twenty-two of the studies were included. The results from the cyclic fatigue tests obtained were in different formats as either the number of cycles to fracture, or time to fracture so studies are grouped together but did not provide an easy comparison (See Appendix A & B).

4.1.3. Excluded studies

Eight studies are excluded (Table 4.3), the most common reason for exclusion was that files studied are not in the inclusion list. Other reasons were that studies had tests carried out at room temperature and the files were immersed at intracanal temperature for only few minutes before. One of the studies excluded was a dissertation in which there was no mention of temperature at which the test was carried out.

Table 4.3. The excluded studies and the reasons for exclusion (The author's own work, 2019).

Study (Author and year of publication)	The reason for exclusion
Du Preez, H. 2014 (Dissertation)	Files studied are not in rotary file list (3.5).
Huang et al.,2017	Austenitic files.
Keles et al., 2019	Immersed at temperature for a few minutes before the test but fatigue test conducted at room temperature.
Pedulla et al., 2011	Non-martensitic files and date.
Shen et al., 2018	Non-martensitic files or not in file list .
Tra ,C. 2017(Dissertation)	No mention of temperature.
Uslu et al., 2018	Not in the list of files.
Uslu et al., 2018	Immersed at temperature for a few minutes before the test but fatigue test conducted at room temperature.

4.2. Methodological Quality

Table 4.4. shows the studies assessed by Joanna Briggs Checklist for Cohort studies (Joanna Briggs Institute, 2019). The table shows results as a score out of ten and the quality of each study is judged by a score. A quality score of 1- 4 is judged as low, 5 - 7 as moderate and 8 - 10 as high. Six of the studies scored 5/10 whilst sixteen scored 6/10. When studies are grouped together, the overall quality of studies is judged as moderate (Table 4.5).

Table 4.4. Quality scores of studies using Joanna Briggs Checklist for cohort studies. Adapted from "Critical appraisal checklist for cohort studies. JBI reviewer's manual," by Joanna Briggs Institute, 2019, (https://wiki.joannabriggs.org/display/MANUAL/Appendix+7.1++Critical+appraisal+checklist+for+cohort+studies).

ID	JB1	JB2	JB3	JB4	JB5	JB6	JB7	JB8	JB9	JB10	Score
1	Yes (1)	NA (0)	NS (0)	NS (0)	NO (0)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	5/10
2	Yes (1)	NA (0)	NS (0)	NS (0)	Yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
3	Yes (1)	NA (0)	NS (0)	NS (0)	Yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
4	Yes (1)	NA (0)	No (0)	No (0)	Yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
5	Yes (1)	NA (0)	NS (0)	NS (0)	no (0)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	5/10
6	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
7	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
8	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
9	Yes (1)	NA (0)	NS (0)	NS (0)	No (0)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	5/10
10	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
11	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
12	Yes (1)	NA (0)	NS (0)	NS (0)	no (0)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	5/10
13	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
14	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
15	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
16	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
17	Yes (1)	NA (0)	NS (0)	NS (0)	no (0)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	5/10
18	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
19	Yes (1)	NA (0)	NS (0)	NS (0)	No (0)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	5/10
20	Yes (1)	NA (0)	No (0)	No (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
21	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
22	Yes (1)	NA (0)	NS (0)	NS (0)	yes (1)	NA (0)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	6/10
Key for Score. Yes =1, NA(not applicable)= 0,NS (Not Stated)=0, No=0.											

Table 4.5. Overall Quality results of studies (The author's own work, 2019).

Score	Quality of studies	Number of Studies
1-4	Poor	0
5 out of 10	Moderate	6
6 out of 10	Moderate	16
7 out of 10	Moderate	0
8-10	High	0

Table 4.6. Bias in the primary studies (The author's own work, 2019).

Risk of Bias	Level of Risk	Comments
Random Sequence Generation (selection Bias)	Low	In studies selected the specimens were randomly allocated to groups.
Representation of samples in relation to target population (Selection Bias)	High	Cyclic fatigue testing methods vary and may not simulate clinical environment. Studies use steel, ceramic or three-point bending tests. Some use custom-made canals or hollow tubes.
Allocation Concealment (allocation Bias)	High	Not stated in any studies. Two studies mention that the tests were carried out by a single operator (Alfawaz et al., 2018; Algahtani, 2018)
Blinding of Participants (Performance Bias)	NA	Cannot be done due to nature of study as participants are metal files.
Blinding of Outcome assessment (Detection Bias)	Moderate /high	No blinding of assessors mentioned in any studies.
Incomplete Outcome Data (Attrition Bias)	Low	No study was found with incomplete data.
Selective Outcome Reporting (Reporting Bias)	Low/ moderate	Three studies detected . Klymus et al., (2018) reported outcomes as time to fracture in seconds rather than number of cycles to fracture to make results seem significant in the absence of findings. Arias, Macorra, Govindjee & Peters (2018) reported in time to fracture in seconds even though different speeds were used. Keles et al., (2019) use mean life in seconds for comparing reciprocating instruments, "Reciproc all" program operates at a speed of 300 rpm and "WaveOne all" program operates at 350 rpm.

The risk of bias in primary studies was assessed (Table 4.6). The risk of random sequence generation is judged as low as files are allocated into groups randomly. There was no mention of the operator being blind from the type of file used in any studies. Two studies (Alfawaz et al., 2018; Algahtani, 2018) mention a single operator performing the entire experiment which prevents any blinding, so the risk of allocation bias is considered high. The blinding of participants cannot be carried out due to the nature of the study being on metal files so marked as not applicable. None of the studies mentioned blinding of outcome assessors so this bias is considered to be high. The risk of incomplete data is judged to be low as no study was found to have incomplete data. The outcome reporting bias is the reporting of some outcomes and not others. This is judged to be moderate as three studies (Arias, Macorra, Govindjee & Peters, 2018; Keles, Eymirli, Uyanık & Nagas, 2019; Klymus et al., 2018) showed reporting of results in time to fracture where the number of cycles to fracture may have been more relevant. Authors may support their findings with relevant citations omitting studies that do not support their findings.

Sample Size calculation

Only seven out of twenty-two studies showed sample size calculation (Table 4.7). A failure to mention sample size calculation methods was taken to mean that it was not done.

Table 4.7. Studies which included sample size calculation (The author's own work, 2019).

ID	Author & Date	Title
10	Erik and Ozyurek, 2018.	Effects of etidronate, NaOCl, EDTA irrigation solutions and their combinations on cyclic fatigue resistance of nickel-titanium single-file rotary and reciprocating instruments at body temperature .
11	Keles et al., 2019.	Influence of static and dynamic cyclic fatigue tests on the lifespan of four reciprocating systems at different temperatures.
13	Klymus et al., 2018.	Effect of temperature on the cyclic fatigue resistance of thermally treated reciprocating instruments.
16	Serafin et al., 2019	In vitro comparison of cyclic fatigue resistance of two rotary single-file endodontic systems: OneCurve versus OneShape.
18	Staffoli et al., 2018	Influence of environmental temperature, heat-treatment and design on the cyclic fatigue resistance of three generations of a single-file nickel-titanium rotary instrument.
20	Algahtani, 2018. (thesis)	Cyclic Fatigue of ProTaper Gold in single and double Curvature Canals.
22	Inan et al., 2019.	Cyclic fatigue of Reciproc Blue and Reciproc Instruments exposed to intracanal temperature in simulated severe apical curvature.

Statistics

There were various statistics used which are judged to be appropriate. Motulsky, (2016) suggested tests such as Shapiro-Wilk or the alternative test Kolmogorov Smirnov can be used to see if the distribution of data, such as number of cycles to fracture from the test, deviates from a comparable normal distribution or normality. This leads to the choice of the next test. If two variables are being measured, then t-tests or Mann-Whitney tests are used depending if tests follow normality or not (Table 4.8); for normality parametric statistics is applied in the form of t-test but if no normality is seen, then non-parametric statistics are applied like Mann-Whitney (Motulsky, 2016). Non-parametric data is when data does not follow normal distribution or a bell shaped symmetrical graph (Grech & Calleja, 2018). If there are three variables of continuous data, then One Way analysis of variance (ANOVA) or alternative test Kruskal Wallis tells significance by comparing two or more groups (usually at least three groups). After ANOVA, it is common to run a Tukey test which tells exactly where the difference lies, by comparing each group's mean with every other group's mean. A 3-way ANOVA shows the interaction between the three variables (Motulsky, 2016).

Table 4.8. Parametric and non-parametric tests. From "WASP (Write a scientific paper): Parametric vs non-parametric tests," by Grech & Calleja, 2018, *Early Human Development,* 123, p.49.

Some commonly used parametric tests and their non-parametric equivalents.

	Parametric test	Non-parametric test
Correlation	Pearson	Spearman/Kendall and others
Two groups, independent measures	*t*-test	Mann-Whitney *U* test (also known as Wilcoxon rank-sum test)
More than two groups, independent measures	One-way analysis of variance (ANOVA)	Kruskal-Wallis test
Repeated measures	Paired *t*-test	Wilcoxon signed-rank test

Most studies used Kruskal Wallis or One-Way ANOVA (Table 4.9). Some used t-tests, three way ANOVA and three studies used Weibull Analysis which measures instrument life. However, the value of Weibull analysis given the variation between cyclic fatigue tests and the clinical environment is uncertain.

Table 4.9. Statistic tests used in studies (The author's own work, 2019).

Study ID	Statistics
1	Kolmogorov-Smirnov test. One-way ANOVA. Tukey HSD test.
2	Weibull Analysis
3	Weibull Analysis
4	Shapiro-Wilk test. Kruskal Wallis. Mann-Whitney tests
5	Shapiro-Wilk. Levene test .One-way ANOVA. Tukey post hoc analysis.
6	t-test (NCF between temperatures) One-way ANOVA& Scheffe post hoc test (within temperature groups)
7	One-way ANOVA. Tukey post hoc analysis.
8	One-way ANOVA. Tukey post hoc analysis.
9	Kruskal Wallis H test. Mann-Whitney U test.
10	Shapiro Wilk . univariate ANOVA. Tukey test.
11	Kolmogorov-Smirnov test. three-way ANOVA. Tukey HSD test.
12	Shapiro Wilk test. One-way ANOVA. Tukey HSD test.
13	One-way ANOVA. Tukey test.
14	One-Way ANOVA. Bonferroni test.
15	Shapiro-Wilk. Levene test .One-way ANOVA. Bonferroni test.
16	Shapiro-Wilk. Levene. T-test.
17	Shapiro-Wilk. T-test. Tukey test.
18	Shapiro-Wilk. One-Way ANOVA.
19	Shapiro-Wilk. Kruskal Wallis test.
20	Kolmogorov-Smirnov test. Levene test. T-test.
21	t-test. One-Way ANOVA. Weibull Analysis
22	Shapiro-Wilk. T test. Weibull analysis.

4.3. Actual Results

The lack of standardisation of cyclic fatigue tests makes it difficult to compare results from different tests. The data extraction tables (see Appendix A & B) show that the variation in the testing methods and information from the cyclic fatigue tests cannot be compared due to lack of standardisation. A list of the included studies is presented in Table 4.10. A PICO data extraction table is presented as table 4.11.

Table 4.10. List of Included studies (Author's own work, 2019).

ID	Author & Year	Title
1	Adiguzel et al., 2018.	Comparison of cyclic fatigue resistance of XP-endo Shaper, HyFlex CM, FlexMaster and RaCe instruments.
2	Arias et al., 2018.	Variable impact by ambient temperature on fatigue resistance of heat-treated nickel titanium instruments.
3	Arias, Macorra, Govindjee & Peters, 2018.	Correlation between temperature-dependent fatigue resistance and Differential Scanning Calorimetry Analysis for 2 contemporary rotary instruments.
4	Alfawaz et al., 2018.	Effects of sodium hypochlorite concentration and temperature on cyclic fatigue resistance of heat-treated nickel-titanium rotary instruments.
5	Azim et al., 2018.	Comparison between single-file rotary systems: Part 2 -The effect of length of the instrument subjected to cyclic loading on cyclic fatigue resistance.
6	De Vasconcelos et al., 2016.	Evidence for reduced fatigue resistance of contemporary rotary instruments exposed to body temperature.
7	Dosanjh et al., 2017.	The effect of temperature on cyclic fatigue of nickel-titanium rotary endodontic instruments.
8	Elnaghy & Elsaka, 2018.	Cyclic fatigue resistance of One Curve, 2 Shape, ProFile Vortex, Vortex Blue and RaCe nickel-titanium rotary instruments in single and double curvature canals.
9	Elnaghy & Elsaka, 2018.	Cyclic fatigue resistance of XP-endo Shaper compared with different nickel-titanium alloy instruments.
10	Erik and Ozyurek, 2018.	Effects of etidronate, NaOCl, EDTA irrigation solutions and their combinations on cyclic fatigue resistance of nickel-titanium single-file rotary and reciprocating instruments at body temperature.
11	Keles et al., 2019.	Influence of static and dynamic cyclic fatigue tests on the lifespan of four reciprocating systems at different temperatures.
12	Keskin et al., 2018.	Cyclic fatigue resistance of XP-Endo Shaper, K3XF and ProTaper Gold nickel-titanium instruments.
13	Klymus et al., 2018.	Effect of temperature on the cyclic fatigue resistance of thermally treated reciprocating instruments.
14	Plotino et al., 2017.	Influence of temperature on cyclic fatigue resistance of ProTaper Gold and ProTaper Universal rotary files.
15	Plotino et al., 2018.	Cyclic fatigue of Reciproc and Reciproc Blue nickel-titanium reciprocating files at different environmental temperatures.
16	Serafin et al., 2019.	In vitro comparison of cyclic fatigue resistance of two rotary single-file endodontic systems: OneCurve versus OneShape.
17	Silva et al., 2018.	Cyclic and torsional fatigue resistance of XP-endo Shaper and TRUShape instruments.
18	Staffoli et al., 2018.	Influence of environmental temperature, heat-treatment and design on the cyclic fatigue resistance of three generations of a single-file nickel-titanium rotary instrument.
19	Yilmaz et al., 2019.	Comparison of cyclic fatigue resistance of One Curve, Hyflex EDM, WaveOne Gold and Reciproc Blue nickel-titanium rotary files at intracanal temperature.
20	Algahtani, 2018.	Cyclic fatigue of ProTaper Gold in single and double curvature canals.
21	Elnaghy & Elsaka, 2016.	Effect of sodium hypochlorite and saline on cyclic fatigue resistance of WaveOne Gold and Reciproc reciprocating instruments.
22	Inan et al., 2019.	Cyclic fatigue of Reciproc Blue and Reciproc Instruments exposed to intracanal temperature in simulated severe apical curvature.

4.11. Data Extraction table using PICO (The author’s own work, 2019).

ID	Population	Intervention	Comparator	Outcome
1	Files: XP-endoShaper Hyflex CM FlexMaster RaCe	The Cyclic fatigue test is carried out at 37 °C in a stainless steel canal of diameter 1.5 mm, 60° angle of curvature and 3 mm radius of curvature.	No control temperature group. The test compared mixed phase (XP-EndoShaper) with austenitic files like Hyflex CM, FlexMaster and RaCe. All are rotary files & of the same size. The files are operated at different speeds and taper varied.	XP-EndoShaper had a greater number of cycles to failure than the other files tested. XP-endoShaper had a greater resistance to cyclic fatigue.
2	Files: Vortex Blue Edge Sequel Sapphire	Cyclic Fatigue test using 3-point bending test used a curvature angle of 60°, the radius of curvature 3 mm and distance of the curve from the tip of the instrument 4.5 mm.	The temperature at room 21 °C (control) and body temperature 37 °C using a water bath.	Vortex Blue instruments were significantly more resistant to cyclic fatigue. Immersion in water at body temperature reduced the cyclic fatigue resistance of all files tested.
3	Files: HyFlex EDM TRUShape	Cyclic Fatigue test using 3-point bending test having 60° curvature angle with the radius of curvature 3 mm and distance of the curve from the tip of the file is 5 mm.	The temperature at room 22 °C (control) is compared to body temperature 37 °C using a water bath. The files have a variable taper with Hyflex EDM having a maximum taper of 0.08 and TRUShape 0.06.The comparison of changes in states of metal at different temperatures. At body temperature comparison of austenitic file (TRUShape) versus martensitic (Hyflex EDM).	HyFlex EDM had a greater number of cycles to failure than TRUShape. HyFlex EDM had the same state of martensitic or r-phase at room and body temperature whilst TRUShape has a mixed phase at room temperature and austenitic phase at body temperature.
4	Files: ProTaper Gold	Cyclic Fatigue Test in a stainless-steel canal wider than PTG F2 file by 0.1 mm, curvature angle is 60° with 5 mm radius, 5 mm distance of curvature from the tip of instrument. Immersed in a bath of different solutions.	The temperature is 25 °C (Control) compared to 37 °C and 60 °C. Different solutions such as distilled water(control) compared with 2.5 % NaOCl and 5.25 % NaOCl.	Higher concentrations of sodium hypochlorite and higher temperature reduced the cyclic fatigue resistance of ProTaper Gold.

5	Files: Hyflex EDM ProTaper Universal WaveOne Gold XP-endoShaper	Cyclic fatigue test in a stainless steel canal 1.5 mm wide, having a curvature angle of 90° and the radius of curvature 3 mm. The distance of the tip of instrument from curvature varies depending on insertion depth of file into canal being 5, 7 or 9 mm.	No comparison temperature, test is carried out at 37 °C. A comparison between martensitic phase files like WaveOne Gold, Hyflex EDM & XP-endoShaper vs conventional austenitic like Protaper Universal (control). Different insertion lengths of file used 15,17 or 19 mm. There are variations in taper, speed & kinematics of the files. Hyflex EDM at 500rpm. ProTaper Universal 300rpm. WaveOne Gold in reciprocation. XP-endoShaper at 1000rpm & 3000rpm.	XP-Endo Shaper had the highest cyclic fatigue resistance compared with all the other instruments, followed by HyFlex EDM, WaveOne Gold and ProTaper Universal. There was no difference between XP-EndoShaper operated at different speeds and at different insertion lengths. However, the other files showed a reduction in cyclic fatigue as the length of the file inserted into the canal increased.
6	Files: ProTaper Universal Hyflex CM TRUShape Vortex Blue	Cyclic Fatigue test using 3-point bending test having 60° curvature angle with radius of the curvature 3 mm and distance of the curve from the tip of instrument 4.5 mm. The working length of the file is 19 mm.	The temperature at room (control) 20 °C compared with 37 °C. There are variations in taper 0.06 vs 0.08 and speed 300 rpm(ProTaper Universal) vs 500 rpm (Vortex Blue and HyflexCM). ProTaper Universal austenitic at both temperatures, others martensitic at room temperature and more austenitic at 37 °C.	At 37 °C HyFlex CM and Vortex Blue had similar cyclic fatigue resistance and higher resistance than TRUShape or ProTaper Universal. Body temperature was associated with a decrease in cyclic fatigue of all files tested.
7	Files: Vortex Blue EdgeFile EndoSequence	The test used a stainless steel canal, which is 1.5 mm wide, having a canal curvature of 90°, the radius of curvature 5 mm. The taper and size of instruments is the same at taper 0.04 and tip size 30 operated at 500rpm.The file length is 25 mm.	The temperature at room 22 °C (control) compared with 3 °C,37 °C and 60 °C. Comparison: Edgefile is martensitic at room temperature, EndoSequence and Vortex Blue more austenitic at room temperature but may become martensitic on cooling. Endosequence is austenitic at body temperature.	EdgeFile had the highest cyclic fatigue resistance followed by Vortex Blue and then EndoSequence. Increasing the temperature decreased the cyclic fatigue resistance of all the files.

8	Files: OneCurve 2Shape Vortex Blue Profile Vortex RaCe.	Test in a stainless-steel canal which has size 30 and 0.08 taper. The curvature angle was 60° with 5 mm radius in the canals with single curvature 6 mm from tip . Double curvature had first curvature angle of 60°, 5 mm radius of the curvature , 8 mm from tip and second curve 70°, 2 mm radius, 2 mm from tip.	The comparison is single curvature (control) versus double curvature canals. 37 °C temperature with no other comparison. The files are immersed in saline and have same taper 0.06 and size at 25. Files which are austenitic like Profile Vortex(control) and RaCe (control) compared to Vortex Blue (mixed) 2shape(austenitic) and OneCurve (martensitic).	The cyclic fatigue of Vortex Blue was greater than the rest of the files tested. One Curve and 2Shape showed better resistance to cyclic fatigue than Profile Vortex and RaCe Files.
9	Files: XP-endoShaper Vortex Blue Hyflex CM iRaCe TRUShape	Cyclic Fatigue test using 3-point bending test having curvature angle 60° with the radius of the curvature 3 mm at 37 °C.	37 °C. There are variations in taper 0.01, 0.04 and 0.06. iRaCe from conventional alloy (control) compared to Hyflex CM, Vortex Blue and TRUShape heat treated alloys and EndoShaper (MaxWire^{tm}).	XP-endo Shaper displayed a greater cyclic fatigue resistance compared HyFlex CM, Vortex Blue, iRaCe and TRUShape files.
10	Files: Reciproc Blue WaveOne Gold Hyflex EDM (HEDM)	Cyclic fatigue tests using custom made ceramic canals at 60° curvature and 5 mm radius of curvature at 37 °C with 25/0.08 size for Reciproc Blue and HyFlex EDM and 25/0.07 for WaveOne Gold. File inserted to 16 mm length.	No temperature comparison just 37 °C. Size at 25, taper 0.08 and 0.07 (WaveOne Gold) but custom made canals. Immersed in 5 solutions. distilled water (control). 6%NaOCl.17%EDTA. 18%HEBP.6%NaOCl+18 %HEBP.Reciprocation (Reciproc Blue and WaveOne Gold) vs continuous rotary (HEDM).	HyFlex EDM had higher resistance to cyclic fatigue in all conditions tested. The combination of HEBP and NaOCl reduced the cyclic fatigue of the files but the other solutions on their own did not have an effect .
11	Files : WaveOne WaveOne Gold Reciproc Reciproc Blue	The cyclic fatigue test is carried out in a steel canal of 1.5 mm width having a curvature angle of 60° & 5 mm radius of curvature. The static file is inserted 20 mm but dynamic inserted 17 mm & moved vertically 3 mm every 2 seconds.	The temperature set at 22 °C (control) compared to 35 °C. The Size of files 25 but taper 0.07 (WaveOne) and 0.08 (Reciproc). Austenitic vs martensitic (blue and gold). Tests static (control) versus dynamic at both temperatures. Reciprocating files have variation in angle and speed of rotation.	In the dynamic model the cyclic fatigue resistance increased. WaveOne showed significantly less cyclic fatigue resistance than the other files tested. There was no difference in cyclic fatigue at different temperatures.

12	Files: XP-endoShaper ProTaper Gold K3XF	Cyclic Fatigue Test with a stainless steel canal 1.4 mm diameter with canal curvature 60°and 5 mm radius of curvature. There is no mention of distance of tip of file from curvature. 19 mm canal length mentioned.	K3XF (control) is austenitic compared to ProTaper Gold and XP-EndoShaper (martensitic). XP-EndoShaper at different speed and torque (800rpm,1Ncm) from the other files which are at 300rpm and 3Ncm. There is variation in taper of files 0.01, 0.09 and 0.04 but size same at 30. No control or comparison temperature was used, just 35 °C.	The XP-endoShaper file had the highest cyclic fatigue resistance compared to ProTaper Gold and K3XF files. Small taper and core may contribute to increased cyclic fatigue resistance of this file.
13	Files: Reciproc Blue X1-Blue WaveOne Gold	Cyclic Fatigue test with stainless-steel custom-made canals with a degree of curvature of 60°, the radius of the curvature 5 mm and 5 mm distance of the curvature from the tip of the instrument.	The temperature at 20 °C (control) compared with 37 °C. The files vary in taper Reciproc Blue 0.08, X1-Blue 0.06 & WaveOne Gold 0.07 but all Size 25, reciprocating, mixed or martensitic phase so no control for comparison. Reciprocating files X1-Blue & WaveOne Gold using WaveOne all program and Reciproc Blue using Reciproc all program .	Body temperature showed a reduction in cyclic fatigue resistance but no significant difference between the files tested. WaveOne Gold showed the least change in the number of cycles to fracture between the temperatures tested.
14	Files: ProTaper Universal ProTaper Gold	Cyclic Fatigue test with stainless-steel custom-made canals with curvature angle 60° and the radius of curvature 5 mm. The files had the same taper, size & speed at 300 rpm. There is no mention of distance of the curve from the tip of file.	The temperature of 20 °C (control) compared with 35 °C. The test compared files size S1 (size 18, taper 0.02) and F2 (size 25, taper 0.08) of both file systems. The test compared austenitic file ProTaper Universal (control) to martensitic file ProTaper Gold.	Intracanal temperature influenced ProTaper Universal files but did not have a significant effect on ProTaper Gold files.
15	Files: Reciproc Reciproc Blue	Cyclic Fatigue test with stainless-steel canals with a curvature angle of 60°, the radius of curvature 5 mm and 6 mm distance of curvature from the tip of the instrument.	The temperature at 20 °C (control) compared to 0 °C, 35 °C and 39 °C. The files have the same variable taper of 0.08 and size of 25.The movement of file systems is reciprocation (Reciproc all program).	Reciproc Blue had a higher cyclic fatigue resistance than Reciproc. All files were affected by temperature increases from 0°C to 35°C with a lower cyclic fatigue resistance at 35°C.

16	Files: OneCurve One Shape	Cyclic Fatigue test with stainless-steel canals with curvature of 60° and the radius of curvature 5 mm. The working length of the file is 16 mm. There is no mention of distance of the tip from canal curvature.	The temperature at 37 °C with no other comparison. One Curve file speed at 300rpm compared to One Shape at 400rpm. The files are the same size and taper. One Shape made of conventional austenitic NiTi and One Curve made of C-wire, heat treated, martensitic.	One Curve files were more resistant to cyclic fatigue than One Shape files.
17	Files: XP-endoShaper TRUShape	Cyclic Fatigue test with stainless-steel custom canals size 0.4 mm apical diameter and 0.06 taper with a curvature angle of 60°, the radius of curvature 5 mm and 5 mm distance of the curvature from the tip of the instrument.	The temperature was set at 37 °C with no other comparison. TRUShape is austenitic and XP-EndoShaper is also austenitic at 37 °C. Similar swaggering movement in the canal but taper differs 0.01 and 0.06. XP-endo speed & torque of 800rpm, 1Ncm and TRUShape 300rpm, 3Ncm.	XP-EndoShaper has a greater cyclic fatigue resistance than TRUShape files.
18	Files: OneShape OneShape New Generation One Curve	The Cyclic Fatigue test used ceramic custom canals with curvature angle of 60°, the radius of curvature 5 mm and 5 mm distance of curvature from the tip of file. The insertion depth of file is 16 mm.	The temperature at 20 °C(control) compared to 0 °C and 35 °C. The tests compared OneShape (austenitic), OSNG (austenitic) and OneCurve (martensitic). The files have the same taper of 0.06, same size of 25, same speed of 300 rpm & kinematics.	OneCurve files were more resistant to cyclic fatigue failure than OneShape and One Shape New Generation files. Decreasing the temperature from 35 °C to 0 °C increased the cyclic fatigue resistance.
19	Files: WaveOne Gold Reciproc B One Curve Hyflex EDM	Cyclic Fatigue test with stainless steel custom canals with curvature angle of 60°, the radius of curvature 5 mm and 5 mm distance of the curve from tip of file at a temperature of 35 °C. All files have martensitic or mixed phases.	The temperature at 35 °C with no other comparison. Reciprocation (WaveOne Gold and Reciproc) vs continuous rotation (Hyflex EDM and OneCurve). Speed: One Curve at 450 rpm, Hyflex EDM at 500 rpm. The angles of reciprocation vary in programs Reciproc all & Wave one all. Taper of files varies WaveOne Gold 0.07, Reciproc Blue 0.08, OneCurve 0.06 and Hyflex EDM 0.08.	Hyflex EDM files had the greatest resistance to cyclic fatigue followed by WaveOne Gold, Reciproc Blue and One Curve files .

20	Files: ProTaper Universal ProTaper Gold	Cyclic Fatigue Test in a ceramic custom made F1(size 20, 0.07 taper). The curvature angle is 60° with 5 mm radius of curvature in the canals with single curvature. Double curved canals had first curve at 60°, 5 mm radius of curvature and second curve 30°, 2 mm radius and 2 mm from the tip of the file.	No comparison for temperature just 37 °C. ProTaper Universal (control) austenitic file compared to ProTaper Gold martensitic file. The files have the same size, taper and speed and used in continuous rotation . Torque varies ProTaper Gold at 150 gcm and ProTaper Universal at 250 gcm. The files are compared in water (control) and 5% NaOCl.	Cyclic fatigue resistance of ProTaper Gold files is greater than ProTaper Universal files. Double curvature and 5% NaOCl reduced resistance to cyclic fatigue.
21	Files: Reciproc WaveOne Gold	Cyclic Fatigue test using 3-point bending test having 60° curvature angle with the radius of curvature 5 mm and the distance of curve from tip of instrument 5 mm. The depth of insertion of file is 19 mm.	The temperature is 20 °C(control) and 37 °C. Files are compared in air(control), saline and NaOCl. WaveOne Gold files compared to Reciproc (control) austenitic. However, taper (Reciproc 0.08 and WaveOne gold 0.07) differs and degrees of reciprocation as different programs used. (Wave One all and Reciproc all).	Both instruments showed a decreased cyclic fatigue resistance when immersed in NaOCl and saline but WaveOne Gold had a higher resistance to cyclic fatigue than Reciproc. There was no significant difference in the fatigue resistance between saline and NaOCl solutions.
22	Files: Reciproc Blue Reciproc	The cyclic fatigue test used stainless steel canals with a curvature angle of 90° and the radius of curvature 2 mm.	No comparison for temperature only 37 °C. The test compares Reciproc files which are austenitic (control) to Reciproc Blue martensitic. The files have same taper at 0.08, size 25 & kinematics (Reciproc all at 300 rpm).	Reciproc Blue had a higher cyclic fatigue resistance than Reciproc files.

Descriptive Analysis

Adiguzel, Isken and Pamukcu (2018) compared XP-EndoShaper, RaCe, Hyflex CM and FlexMaster files at 37 °C in a metal canal of 1.5 mm diameter, having an angle of curvature of 60° and the radius of curvature 3 mm, concluding XP-EndoShaper file to have a greater resistance to cyclic fatigue. The comparison (Table 4.11) is between files having mixed phases (XP-EndoShaper) and those having austenitic phases; the study claimed these files can be compared, based on a similar taper of 0.04, that the instruments created in the canal at the end of shaping. XP-EndoShaper file has a serpentine shape in action, or s-shaped movement, that expands to create a canal of this taper but manufacturers state a taper of 0.01 and tip size as small as 15. There is no mention of the distance of the tip of the instrument from the curvature and the files were operated at different speeds. The A_f of Hyflex CM is mentioned to be 47 °C and that of XP-EndoShaper to be around 35 °C stating that it changes from martensite to austenite between 32 – 37 °C so during this test XP-EndoShaper would be in an austenitic phase.

Arias et al. (2018) compared various sizes of Vortex Blue and EdgeSequel Sapphire™ using room temperature of 20 °C as the control, compared with body temperature of 37 °C, in a three-point bending test, having a curvature of 60° with the radius of the curvature 3 mm and distance of the tip of the instrument from the curve 4.5 mm, in a water bath, concluding that Vortex Blue files were significantly more resistant to cyclic fatigue. The files were operated at the same speed with no torque and had the same taper. Arias et al. (2018) mentions that both instruments are in an austenitic state when coming to body temperature but at room temperature Vortex Blue would be in R-phase if being cooled or heated to room temperature, while EdgeSequel Sapphire would be martensitic if being raised to room temperature or mixed if being cooled from a higher temperature. In clinical practice, the temperature of a file changes, when introduced into the canal it is heated up and then as it is removed from the canal and kept on the dentist's tray it starts to cool. The ambient temperature can vary if air-conditioning is present and the files may be cooled considerably if the ambient temperature is low or may be heated if placed near a heat source like a radiator.

Arias, Macorra, Govindjee and Peters (2018) compared Hyflex EDM to TRUShape™ files at room temperature of 22 °C (control) and body temperature 37 °C, in a three-point bending test with a canal curvature angle of 60°, 3 mm radius of curvature and 5 mm distance of curvature from the tip of the file, concluding that Hyflex EDM had a greater cyclic fatigue resistance than TRUShape files and that the cyclic fatigue of Hyflex EDM were unaffected by temperature. However, the study used the mean or average life of the instrument, which calculates the time in seconds but the instruments were operated at different speeds and had different tapers. Hyflex EDM is also normally recommended by the manufacturer to be used at 500 rpm with torque of 2.5 Ncm but the settings used in this study are 400 rpm and no torque. TRUShape files were tested at 300 rpm. The conclusions would be similar if the number of cycles to failure was considered as Hyflex EDM would have a significantly higher number of rotations. Arias et al. (2018) concluded that Hyflex EDM would be in R-phase if coming to 37 °C from above this temperature and martensitic (R-phase and martensitic) if coming to 37 °C from below. The graph (Figure 4.1) shows the R_f temperature of 36.71 °C, then at the intracanal temperature in the range of 31°C - 36 °C, this file would be R-phase or martensitic.

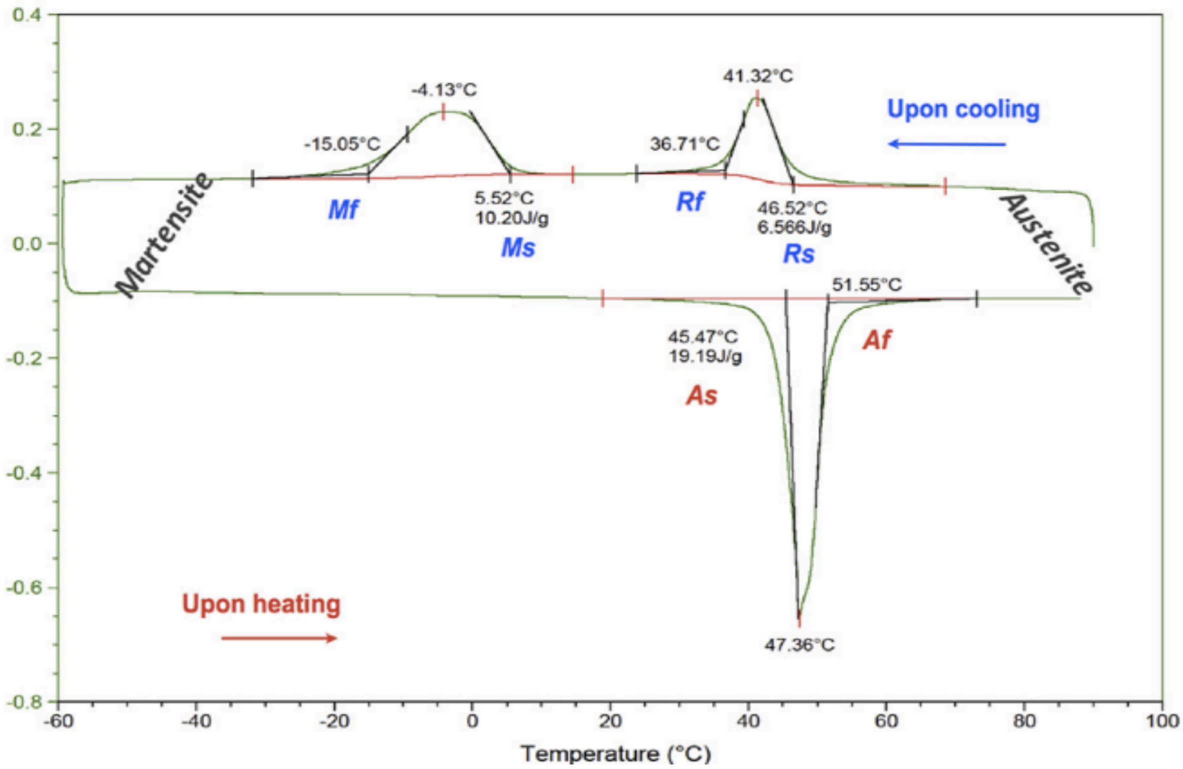


Figure 4.1. Transition temperatures of Hyflex EDM showing M_s, M_f, R_s, R_f, A_s and A_f . From "Correlation between temperature-dependent fatigue resistance and differential scanning calorimetry analysis for 2 contemporary rotary instruments," Arias at al., 2018, *Journal of Endodontics,* 44(4), p. 633.

Alfawaz et al. (2018) examined the effect of sodium hypochlorite on ProTaper Gold files using a control temperature of 25 °C comparing with temperatures of 37 °C and 60 °C in stainless-steel custom-made canals with an angle of curvature 60°, 5 mm radius of curvature which is 5 mm from the file tip in different solutions such as distilled water (control), 2.5 % NaOCl and 5 % NaOCl. However, the effect of galvanic corrosion due to dissimilar metals has made use of ceramic canals more suitable for this type of study. The results of the study showed that cyclic fatigue decreased with increasing temperature and in the presence of NaOCl. The study compared a high temperature of 60 °C which showed reduced fatigue resistance. It is interesting to note that irrigants heated to this level rapidly loose heat in the canal and reach 37 °C within a minute (De Hemptinne et al., 2015); yet to know the effect for a minute would be interesting. This type of variable could be incorporated in a dynamic testing method.

Azim, Tarrosh, Azim and Piasecki (2018) compared XP-EndoShaper, Hyflex EDM, WaveOne Gold and ProTaper Universal™ at 37 °C, in 90° curved stainless-steel canal, 1.5 mm width with 3 mm radius of curvature with files at three different insertion lengths, 15 mm, 17 mm and 19 mm and found that XP-EndoShaper had the greatest resistance to cyclic fatigue followed by Hyflex EDM, WaveOne Gold and then ProTaper Universal. However, WaveOne Gold is a reciprocating file with speed of 350 rotations per minute but due to the counter-clockwise movement being greater than the clockwise movement, it can be a difficult calculation to make with precision. The rest of the files were operated in continuous rotation. Azim et al. (2018) mention that all files were affected by the position of the curvature moving coronally as the depth of insertion increased, as the stresses are concentrated on the file where its diameter is larger, except XP-Endo Shaper and this could be due to its narrow taper. The cyclic fatigue resistance of XP-EndoShaper was not affected by different speeds used, 1000 rpm and 3000 rpm, or by different lengths of insertion.

De Vasconcelos et al. (2016) compared Hyflex CM, Vortex Blue, TRUShape and ProTaper Universal at 20 °C and 37 °C, finding that Hyflex CM and Vortex Blue showed a similar resistance to cyclic fatigue at 37 °C when compared with ProTaper Universal and TRUShape. De Vasconcelos et al. (2016) measured the surface temperature of rotary instruments when removed from a root canal using an infrared thermometer in a pilot study and found it to be in a range of 30.8 - 32.5 °C. Two previous studies mentioned a wide range of 31– 36 °C (Cunningham et al., 1980; De Hemptinne et al., 2015). This shows a wide variation for intracanal temperature with a further need for research in this area. The DSC revealed that A_f for Hyflex CM is 44 °C suggesting that the conversion to austenite is not complete but a majority of the instrument would be austenitic, with some martensitic R-phases at body temperature. Vortex Blue would be austenitic at body temperature but at intracanal temperature which could be as low as 30.8 °C may be more martensitic at A_s is 30.81 °C, the graph (Figure 4.2) for Vortex Blue showed two dips in the heating phase which may indicate a different phase.

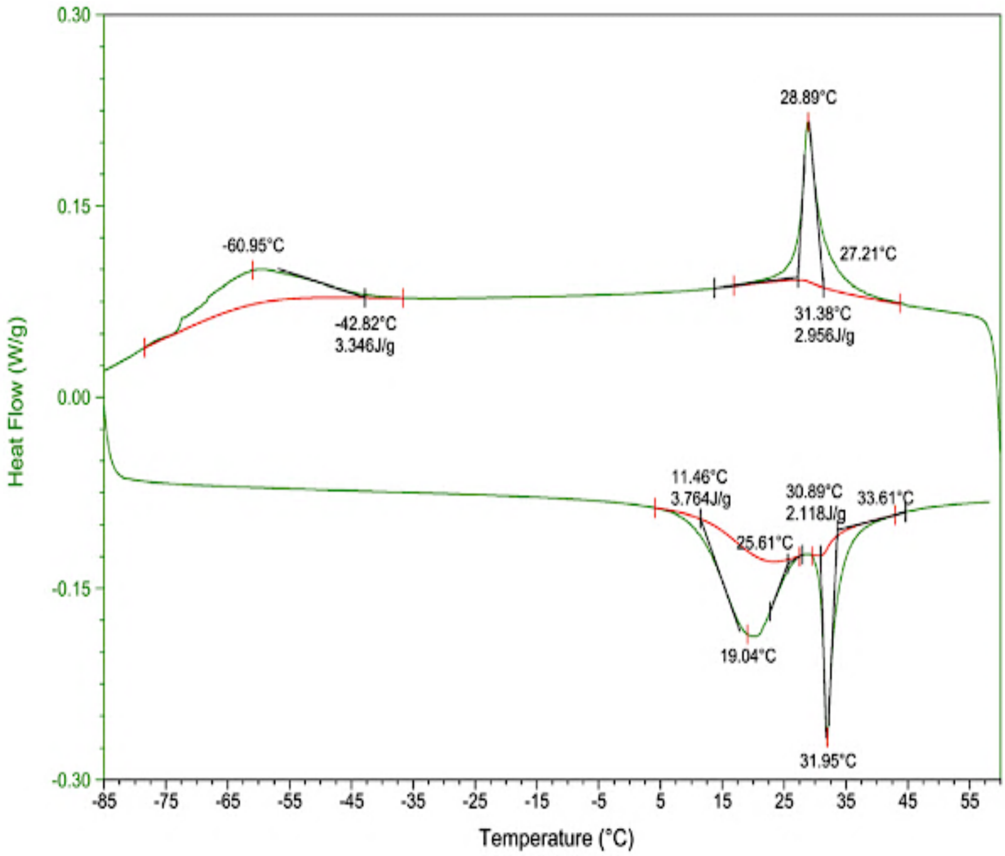


Figure 4.2. DSC curves showing heat flow during cooling (upper trace) and heating (lower trace) of Vortex Blue. From “Variable impact by ambient temperature on fatigue resistance of heat treated nickel titanium instruments,” by Arias et al., 2018, *Clinical Oral Investigations,* 23 (3),p. 1105.

Dosanjh, Paurazas and Askar (2017) studied the effects of various temperatures 3, 22, 37 and 60 °C on the cyclic fatigue resistance of Vortex Blue, EdgeFile™ and EndoSequence, showing that increasing temperature reduced the cyclic fatigue resistance of all files tested, with EdgeFile having the highest resistance to cyclic fatigue followed by Vortex Blue and then EndoSequence. Vera et al. (2015) studied the effects of reducing intracanal temperature by using a chilled irrigant (as cited in Dosanjh et al., 2017) and that it resulted in a 10 °C reduction in external root temperature which could reduce inflammation around the root. Dosanjh et al. (2017) suggested that most cyclic fatigue tests are done on metal blocks but dentine would have different conducting and insulating properties when compared to metal. The study used a hollow tube design of 1.5 mm width with a canal curvature of 60° and radius of curvature 5 mm but there is no mention of the distance of the tip of the instrument from the curvature.

Elnaghy and Elsaka (2018) compared One Curve, 2Shape, Profile Vortex, Vortex Blue and RaCe in single and double curved canals at a temperature of 37 °C, concluding that Vortex Blue had better cyclic fatigue resistance than the other files tested. The tests showed that all files had a lower number of cycles to fracture in double curved canals than in single curvatures. Willerhausen, Kasaj, Röhrig and Marroquin (2008) showed that almost all teeth can have double curvatures (as cited by Elsaka & Elnaghy, 2018), even the ones with a single canal like lower incisors may have double curvatures which may not be visible radiographically as they may not be in the same plane as the radiograph.

Elnaghy and Elsaka (2018) compared the cyclic fatigue of XP-EndoShaper, Hyflex CM, Vortex Blue, iRaCe™ and TRUShape files at 37 °C in a three-bend cyclic fatigue test. The files have a triangular cross section but a varied taper. Hyflex CM is mixed martensitic and austenitic at room temperature and TRUShape is more austenitic than Hyflex CM. The taper of TRUShape at 0.06 reduced its flexibility and corresponding fatigue resistance was less but still greater than iRaCe. XP-Endoshaper had the best resistance to cyclic fatigue but this could be due to its martensitic alloy, small taper of 0.01 and small core size (Figure 4.3).

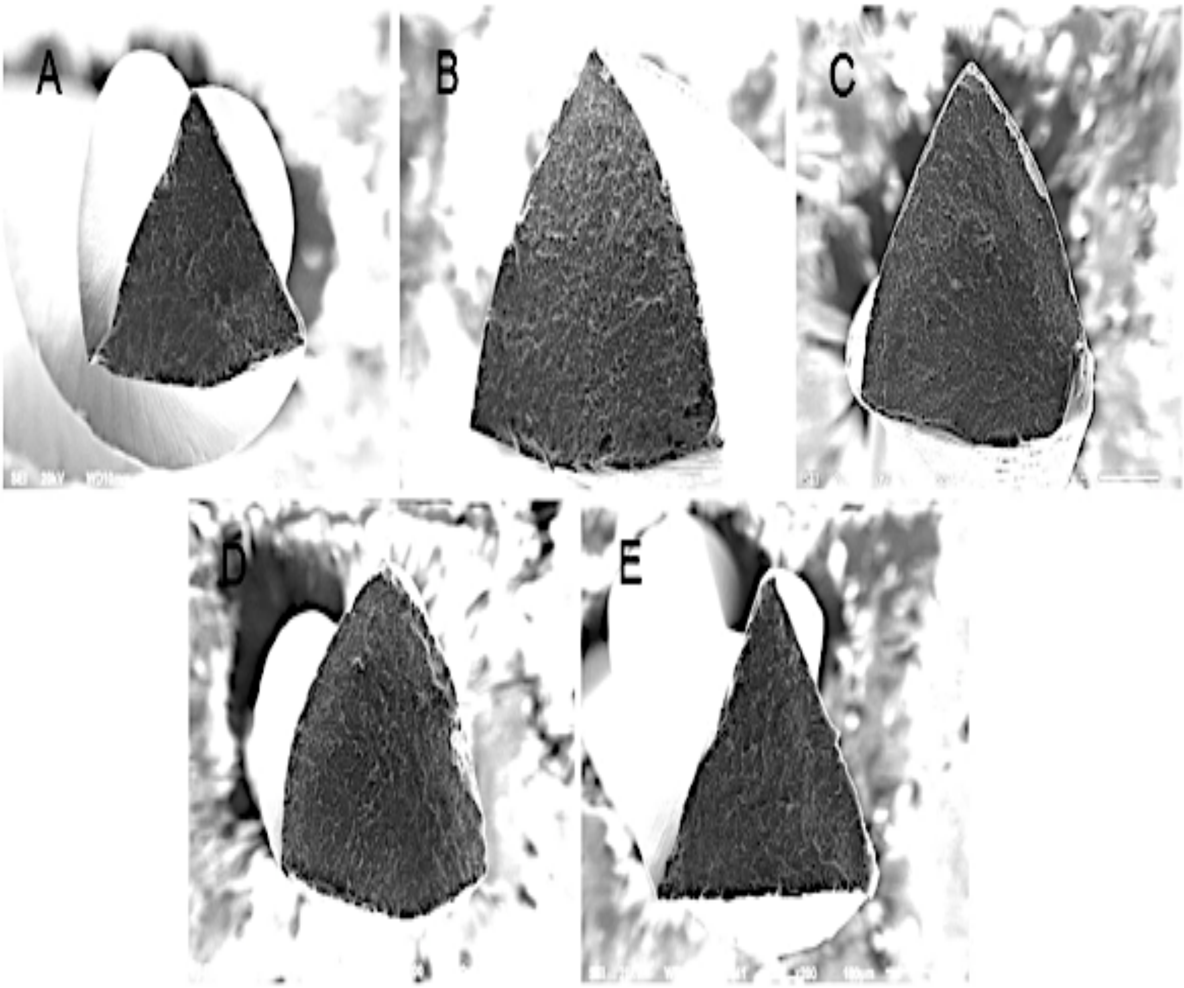


Figure 4.3. Images of fractured surfaces of files showing the small core for XP-EndoShaper a) XP-endoShaper b) TRUShape c) Hyflex CM d) Vortex Blue. From “Cyclic fatigue resistance of XP-Endo Shaper compared with different nickel-titanium alloy instruments,” by Elnaghy and Elsaka, 2018, *Clinical Oral Investigations*, *22*(3), p. 1435

Erik and Ozyurek, (2018) compared three martensitic files which are WaveOne Gold, Hyflex EDM and Reciproc Blue in solutions such as distilled water, 6% NaOCl, 17% EDTA, 18% etidronic acid and a fifth solution which was a combination of 6% NaOCl and 18% etidronic acid at 37 °C. They found that Hyflex EDM performed the best out of all the files in the various solutions tested and that the mixture of etidronic acid and NaOCl caused a reduction in cyclic fatigue resistance but in the other solutions there was no significant effect. The tests were carried out at 37 °C, in custom made ceramic canals according to the taper of the file, with a canal curvature of 60° and the radius of curvature 5 mm. Zehnder et al.

(2005) mention using etidronic acid or HEBP instead of EDTA (as cited in Erik and Ozyurek, 2018), as it does not react with NaOCl, whilst EDTA can reduce the effectiveness of NaOCl when used together (Rossi-Fedele et al., 2012) but Erik and Ozyurek, (2018) showed that the combination of NaOCl and HEBP reduced the cyclic fatigue resistance of all the files tested.

Keles et al. (2019) compared reciprocating file systems WaveOne, WaveOne Gold, Reciproc and Reciproc Blue under static and dynamic tests at temperatures of 22 °C and 35 °C using a metal tube design of 1.5 mm diameter, 60° curvature angle and 5 mm radius of curvature. The dynamic tests were conducted, introducing the files into the canal to a depth of 17mm and then oscillating the file 3 mm vertically every 2 seconds. The files in the dynamic tests were found to have higher cyclic fatigue and temperature was not found to be significant. The dynamic model of testing means that the files have less stress on a particular area as the files are in motion constantly, which translates to longer times to fracture and simulates a clinical environment. In a clinical environment, the oscillations may be a lot lower and varied depending on the operator. Keles et al., (2019) mentions that this study gives conflicting results to previous studies regarding the effect of temperature and this may be due to variation in the methodology in different studies, for example, stainless steel or ceramic canals or using an oven or water baths. This highlights the need for standardisation of cyclic fatigue tests and a need to explore dynamic fatigue testing methods as suggested by the author previously.

Keskin, Inan, Guler and Kalyoncuoğlu (2018) compared ProTaper Gold, K3XF™ and XP-EndoShaper files at 35 °C in a metal tube of 1.4 mm diameter, with a curvature angle of 60° and the radius of curvature 5 mm. The XP-Endoshaper was found to have the greatest cyclic fatigue resistance but it was noted that it is difficult to compare these files as the taper varied. The XP-Endoshaper has a taper of 0.01, whilst K3XF has a 0.04 taper and ProTaper Gold F3 has 0.09 variable taper. The effect of the characteristics of the metal cannot be separated from the small core size of the file and the possibility that the factors combine to create a higher cyclic fatigue resistance for the XP-EndoShaper file.

Klymus et al., (2018) compared Reciproc Blue, X1-Blue™ and WaveOne Gold files at 20 °C and 37 °C in steel custom-made canals with an angle of curvature at 60° and the radius of curvature of 5 mm, concluding that at body temperature, the cyclic fatigue resistance of all files reduced. However, the files were operated at different speeds and had different tapers so the significance of time to fracture cannot be relied upon and the cyclic fatigue resistance when looking at the number of cycles to failure of the different files at 37 °C could be seen to be similar. WaveOne gold showed the least variation between the temperatures tested; with blue files having more austenitic phases than gold files at intracanal temperature as have lower A_f temperatures.

Plotino, Grande, Mercadé Bellido, Testarelli and Gambarini (2017) found that testing at temperatures 20 °C (control) and 35 °C, in a custom-made metal canals having a curvature angle of 60° and the radius of curvature 5 mm, showed a reduced cyclic fatigue resistance of ProTaper Universal files but did not affect ProTaper Gold. The ProTaper Gold files had a higher cyclic fatigue resistance, than the ProTaper Universal files and in both types of files it was seen that files of a larger size had a lower resistance. The higher fatigue resistance was attributed to the two-stage transformation of the gold alloy, which transforms from austenitic to reverse phase and then martensitic. The reverse phase is considered to be a martensitic phase but the alloy has a high A_f near 55 °C so some austenitic phases may be present. It would be interesting to know the A_s temperature and transition temperatures for the R-phase to study the effect of temperature or lack of it on ProTaper Gold files.

Plotino et al. (2018) compared Reciproc and Reciproc Blue at temperatures of 0 °C, 20 °C, 30 °C and 39 °C, in steel canals having a curvature angle of 60°, 5 mm radius of curvature which is 6 mm from the tip of the file, finding that Reciproc Blue had greater cyclic fatigue resistance. As the temperature increased from 0 °C to 35 °C, the cyclic fatigue resistance decreased. The Reciproc Blue files are soft and the transition temperature between the austenitic and martensitic phase is below body temperature. DSC measurements revealed a range of 26.9 - 28.7 °C for A_s and 34.8 – 36 °C for A_f. Grande, Ahmed, Cohen, Bukiet and Plotino (2015) mentioned that there are many variations to reciprocation (as cited in Plotino et al., 2018), there could be a backward or forward movement with degrees of movement being partial or complete; hybrid reciprocation which is combined reciprocation and rotational movements and this can change by a shift from one type of reciprocation to the other in the canal based on mechanical resistance and torque.

Serafin, De Biasi, Franco and Angerame (2019) compared the cyclic fatigue resistance of OneCurve and OneShape files at 37 °C, in stainless-steel custom-made canals with curvature angle 60° and 5 mm radius of curvature, concluding that One Curve files had more resistance to cyclic fatigue. The depth of insertion of the file was 16 mm. Even though the number of rotations is calculated from the time to fracture allows comparison, the files were operated at different speeds, 300rpm for OneCurve and 400rpm for OneShape; the authors of the study mention that the literature suggests that higher speeds reduce the cyclic fatigue resistance, yet the study was carried out at different speeds. One Curve files are made from a heat treated NiTi alloy called C-wire, whilst OneShape is made from conventional austenitic NiTi.

Silva et al. (2018) compared TRUShape and XP-Endoshaper files at 37 °C, in a custom-made canal with an apical diameter of 0.4 mm and 0.06 taper having curvature angle 60°, 5 mm radius of curvature which is 5 mm from the tip of the file and found XP-EndoShaper to have a greater cyclic fatigue resistance. The TRUShape has a similar movement in the canal as an s-shape and Silva et al. (2018) comment that this is the reason the files have been compared even though the taper varies. The speed and torque at which the files are operated varies in this experiment, XP-Endoshaper at 800rpm with the torque at 1Ncm and TRUShape at 300 rpm with the torque at 3 Ncm but the authors of this study mention Pedulla et al. (2014) where speed did not have a significant effect on the cyclic fatigue resistance of the Mtwo™ files.

Staffoli et al. (2018) compared OneCurve, OneShape and One Shape New Generation™ files at temperatures of 0 °C, 20 °C and 35 °C, in custom-made ceramic canals of 60° curvature, 5 mm radius of curvature which is 5 mm from the tip of the instrument; finding OneCurve to have the greatest cyclic fatigue resistance and that as the temperature decreased, the cyclic fatigue resistance of all files increased. The A_f of OneShape files is 10 – 18 °C and One Curve is 40 – 50 °C, so One Curve files are martensitic at room and intracanal temperature, whilst OneShape files are austenitic. It would be interesting to see the transition temperatures of the martensitic phase to verify the amount of martensitic phases in OneCurve files.

Yilmaz, Ozyurek and Uslu (2019) compared OneCurve, WaveOne Gold, Reciproc Blue and Hyflex EDM at 35°C, in custom-made stainless-steel canals with a curvature angle of 60°, both radius and distance of curvature from the tip of the file at 5 mm, concluding that the Hyflex EDM file had the greatest resistance to cyclic fatigue followed by WaveOne Gold, Reciproc Blue and lastly OneCurve files. However, the taper, speed and kinematics varied in the files tested and there are errors in referencing and in the discussion section.

Algahtani (2018) wrote in a thesis on the comparison of cyclic fatigue between ProTaper Gold and ProTaper Universal files, in single and double curved canals, at 37 °C using water and 5 % sodium hypochlorite in ceramic custom-made canals (Figure 4.4). The canals were custom made to match a size F1 file with both single and double-curved canals having 60° curvature and 5 mm radius of curvature but the double canal having a second curve of 30°, 2 mm radius of curvature and 2 mm distance of curvature from the tip of the file. The fatigue life of ProTaper Gold was better than ProTaper Universal and better in water than in NaOCl. Ceramic canals do not wear or corrode allowing more standardisation of testing methods.

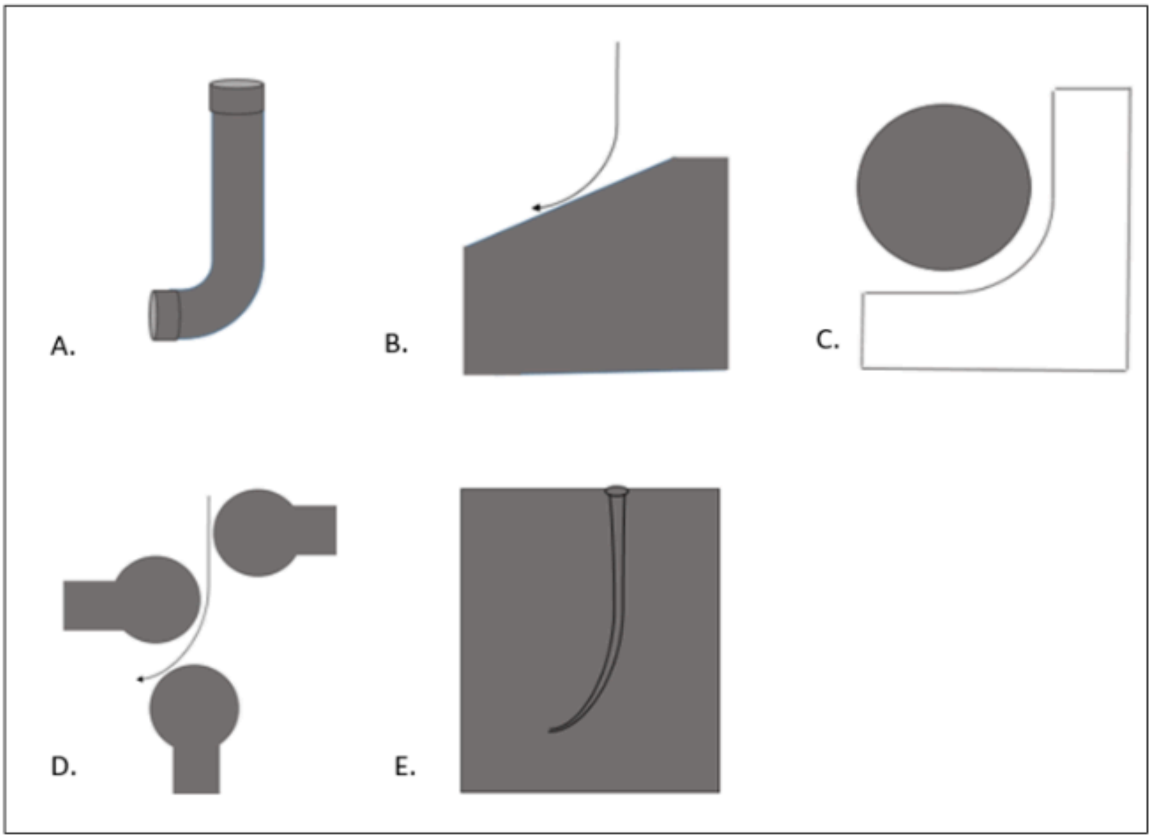


Figure 4.4. Five methods of cyclic fatigue tests. A) hollow metal tube B) inclined plane c) Grooved block d) 3 bend test e) custom made canal. From “Cyclic fatigue of ProTaper Gold in single and double curvature canals, ” by F.N. Algahtani, 2018, Master’s thesis, p. 9.

Elnaghy and Elsaka (2016) compared Reciproc with WaveOne Gold in air, saline at 37 °C and 5 % sodium hypochlorite at 37 °C, in a three-bend test with a curvature angle of 60°, 5 mm radius of curvature and 5 mm distance of the curve from the tip of the file; finding that WaveOne Gold had greater resistance to cyclic fatigue than Reciproc and all files had a lower resistance in 5% sodium hypochlorite and saline. There was no significant difference between saline and sodium hypochlorite solutions and no pitting indicative of corrosion was noticed. However, the taper varied of the files tested with Reciproc at 0.08 and WaveOne Gold at 0.07 and several studies (Sanghvi & Mistry, 2011; Khasnis et al., 2018) show that greater taper can reduce cyclic fatigue resistance. The comparison is made by the number of cycles to fracture and it can be difficult to compare reciprocating instruments in this way as each file system has different angles of movement. Reciproc has a counter-clockwise movement of 150° and a clockwise movement of 30°, whilst WaveOne Gold has a counter-clockwise movement of 170° and a clockwise movement of 50° (Plotino, Grande, Testarelli and Gambarini, 2012). It can be difficult to separate the factors and these may act together, like the design of the files with Reciproc having an s-shaped cross section and WaveOne Gold having a more triangular cross section.

Inan, Keskin, Yilmaz and Baş (2019) compared the cyclic fatigue resistance of Reciproc and Reciproc Blue, at a temperature of 37 °C in a severe (90°) curved stainless-steel canal with 2 mm radius of curvature and found Reciproc Blue to be better at resisting failure from cyclic fatigue. The A_f of Reciproc Blue is 30.73 °C and Reciproc having an A_f of 58 °C. As both files have the same taper, shape and kinematics; the difference can be attributed to metallurgy but the phases present may need further investigation.

Discussion

5.1. Summary

Hyflex EDM file has R-phases and martensitic phases but no austenitic phases present at intracanal temperature as it has R_s of 46 °C and R_f of 36 °C (Arias et al., 2018) and A_s of 42- 43 °C and A_f of 51- 54 °C (Iacono et al., 2017). Intracanal temperature has a wide range 30.8 - 36 °C and more precise data is needed to establish this range (Cunningham et al.,1980; De Hemptinne et al., 2015; De Vasconcelos et al., 2016).

Vortex Blue may be austenitic if intracanal temperature is higher than A_f 33.71 °C (De Vasconcelos et al., 2016; Arias et al., 2018) or it could be changing from one phase to another with R_s of 33.6 °C and R_f of 30.89 °C like XP-EndoShaper file. Reciproc Blue at intracanal temperature, will have austenitic phases as A_f is 30.73 °C (Inan et al., 2019); A_s is 26 – 28 °C and A_f is 34.8 – 36 °C (Plotino et al., 2018) and martensitic phases as R_s is 46.8 °C and R_f is 27.5 °C (Almeida et al., 2019). ProTaper Gold has A_s around 40 °C and A_f around 50 °C, the cooling graph showing possible M_s near 40 °C and M_f near 30 °C (Hieawy et al., 2015), could be martensitic or r-phases but no data exists on R_s and R_f temperatures to confirm this (Hieawy et al., 2015; Aoun et al., 2017). OneCurve could have martensitic phases as A_f is 40 - 50 °C but there is no data on A_s ,M_s and M_f temperatures (Staffoli et al., 2018). Hyflex EDM may be the only true martensitic phase file at intracanal temperatures. XP-EndoShaper may be martensitic if intracanal temperature is kept low as changes phase between 32 – 37 °C but no DSC exists to confirm this (Adiguzel et al., 2018). XP-EndoShaper, Reciproc Blue and Vortex Blue (Adiguzel et al., 2018; De Vasconcelos et al., 2016; Inan et al., 2019; Plotino et al., 2018) show transition temperatures in the range of intracanal temperature and this process of transitioning within the canal may have an effect on cyclic fatigue resistance.

ProTaper Gold does not seem to be affected by room or intracanal temperature as probably in the same phase at both temperatures (Hieawy et al., 2015; Plotino et al., 2017). ProTaper Gold has been suggested to be used in narrow calcified canals as it has a higher torsional resistance than Hyflex EDM (Kaval et al., 2016; Silva et al., 2018). Hyflex EDM files have a greater cyclic fatigue resistance than most other file systems tested in the studies except XP-Endoshaper and should be used in severely curved canals (Arias et al., 2018; Azim et al., 2018; Erik & Ozyurek, 2018; Yilmaz et al., 2019). A combination of factors (Table 5.1) may increase the cyclic fatigue resistance of XP-Endoshaper such as having a taper of 0.01, a small core, MaxWire metallurgy and a swaggering movement in the canal (Adiguzel et al., 2018; Azim et al., 2018; Elnaghy & Elsaka, 2018; Elnaghy & Elsaka, 2018; Keskin et al., 2018; Silva et al., 2018).

Table 5.1. The combination of factors which can affect cyclic fatigue resistance in files which have martensitic phases (The author’s own work, 2019).

Files	Taper	Cross section	Phases	Kinematics	Surface
Vortex Blue	0.06	Triangular. 3-point contact	<33.71 °C Martensitic	Rotary 500 rpm	Titanium oxide layer
Reciproc blue	0.08	s-shaped cross section non-cutting tip 2 cutting edges	R phase & small % of austenite	Reciprocation Reciproc all. 300 rpm	Blue
Wave One Gold	0.07	Parallelogram cross section creating only 1 contact point . Off-centred cross section. Variable and reducing taper	R-phase	Reciprocation WaveOne all program.350rpm	Gold
Protaper Gold	0.08	Convex triangular Progressive variable taper	Martensite	Rotary 300rpm	Gold
Hyflex EDM	0.08	Quadratic apical third Trapezoidal in middle third Almost triangular in the coronal third Variable taper	Martensitic & R-phase	Rotary 500rpm and 2.5 Ncm	EDM rough surface
One Curve	0.06	Triangular at the tip and s-shaped at the shaft	Mixed	Rotary 300rpm	electropolished
XP-Endo Shaper	0.01/ 0.04	Serpentine movement Booster tip with 6 cutting edges . tip 15 -27.	Martensitic austenitic at 32-37°C	Rotary 800rpm 1Ncm	MaxWire Electropolished

Azim et al. (2018) found XP-EndoShaper to have a greater cyclic fatigue resistance than Hyflex EDM and it was not affected by speed (1000 rpm or 3000 rpm) or depth of insertion of the file. However, as this is a single study that was carried out in a 1.5 mm wide canal and not a custom-made canal, the results should be interpreted with caution.

5.2. The completeness and applicability of evidence

The methodology varies which makes comparing studies difficult. There are variations in the angle of curvature and distance of the curve from the tip of the file and some studies do not even mention this. There are various methods of maintaining temperature from ovens to baths and recording the temperature such as a simple thermometer to infrared thermometer. Some tests have controls, some have none. Transition temperatures for the various files varied and could be difficult to find with ProTaper Gold, One Curve and XP-EndoShaper lacking information on detailed transition temperature. There was a wide variation seen in transition temperatures in the various studies which makes it difficult to know the precise phase composition of the files tested.

5.3. Appraisal of Quality of evidence

There has been some poor discussion and errors in referencing in some studies (Alfawaz et al., 2018; Yilmaz et al., 2019). Many of the studies (Adiguzel et al., 2018; Alfawaz et al., 2018; Arias et al., 2018; Azim el al., 2018; De Vasconcelos et al., 2016; Dosanjh et al., 2017; Elnaghy & Elsaka, 2016; Elnaghy & Elsaka, 2018; Keskin et al., 2018; Plotino et al., 2017; Plotino et al., 2018; Silva et al., 2018; Yilmaz et al., 2019) had no mention of how sample size was calculated or if it had been estimated from other studies; this can be an important factor as it can make relevant findings seem insignificant or significant findings seem insignificant. This indicates the need for standardisation on both static and dynamic cyclic fatigue tests.

In a number of studies, it is difficult to single out the intervention as factors act together may be specific to the file such as taper, speed, kinematics and metallurgy. Cyclic fatigue tests lack standardisation and have many variables; the scoring system of quality fails to take this into consideration. Blinding of operators and blinding of outcome assessors could improve quality scores and show higher quality scores but in the absence of ways to measure the other variables, it would not be accurate. The Joanna Briggs checklist also fails to consider a sample size calculation.

5.4. Potential Bias in the review process

The risk of bias during the review process is assessed under the various categories in table 5.2. As the review found a few dissertations on the topic and one met the criteria for inclusion, the risk of publication bias is judged as moderate. Language Bias could occur as the inclusion criteria restricted studies to English. However, the searches only found one study in Chinese, which would have been excluded on language but a translation for the abstract was found later so it was also excluded on inclusion criteria. Therefore, the potential risk of language bias is judged to be low.

Table 5.2. Bias in Systematic review (Authors own work; 2019).

Type of Bias	Risk	Comments
Publication	Moderate	Efforts were made to search and include grey literature. However, only electronic databases and studies in English were included.
Language	Low	Although only studies in English were included, only one study was found in Chinese which was excluded when a translated abstract to English was found.
Time lag	Unknown	
Funding	Low	No funding involved.
Citation	Low	Effort made to screen articles but no relevant articles found.
Location	High	Electronic databases searched.
Search	High	Single reviewer.
Duplicate publication	Low	All screened and no similar studies found.
Abstract to full text	Low	Both abstracts and full texts screened.
Outcome reporting Bias	High	Single reviewer.

The risk of a time lag bias is difficult to judge. As no funding was involved in this review, the risk of funding bias is judged as low. Citation bias can occur due to the primary authors citing works that confirm their opinions and if looking at the reference lists of primary articles then this can get duplicated in a systematic review (Higgins & Green, 2011). However, no studies were identified during the citation searches, so the risk remains low. Location bias can occur, as electronic databases and mainstream journals such as Journal of Endodontics were used so the risk of this bias remains high. Search bias is judged to be high as a single reviewer undertook the searches and created the search terms. Abstract to full text bias is considered low as all full texts were available and searches included both. Duplicate publication bias can occur when the same study is published more than once in different journals and can lead to overestimation of positive results (Higgins & Green, 2011). As the studies were screened for duplicates at all stages, this risk is judged to be low. The outcome reporting bias is judged as high as a single reviewer has reviewed the studies.

5.5. Agreement or disagreement with other studies or reviews

There are no previous reviews on cyclic fatigue tests on martensitic phase files. There is a wide range for intracanal temperature from 30.8 – 36 °C (Cunningham et al.,1980; De Hemptinne et al., 2015; De Vasconcelos et al., 2016) due to lack of recent research into measuring intracanal temperature and the variables affecting it. Keles et al. (2019) showed that temperature did not affect dynamic cyclic fatigue tests and is not in agreement with earlier studies but it highlights the need for standardisation of cyclic fatigue testing systems in terms of static and dynamic tests. Most studies (Alfawaz et al., 2018, De Vasconcelos et al., 2016; Dosanjh et al., 2017; Klymus et al., 2018; Plotino et al., 2018; Staffoli et al., 2018) showed a decreased cyclic fatigue resistance at intracanal temperatures which is in agreement with earlier studies (Campbell et al., 2014) but these studies are using static testing methods. The martensitic phase files showed an increased resistance to cyclic fatigue compared with other files tested. The increased cyclic fatigue resistance of martensitic files like Hyflex EDM was in agreement with previous studies (Pirani et al., 2016; Kaval et al., 2016) . Files used in reciprocation such as WaveOne Gold did not have an increased resistance when compared to Hyflex EDM but it is difficult to measure this separately from other factors which influence cyclic fatigue resistance.

Conclusion

Within the limitations of this study, it was seen that the martensitic phase files had a better resistance to cyclic fatigue in all the in vitro tests. It is found that Hyflex EDM is a martensitic file, having martensitic and R-phase which is considered to be a martensitic phase (Iacono et al., 2017; Arias et al., 2018). It has a greater resistance to cyclic fatigue than most of the files tested, except the XP-EndoShaper file, allowing it to be used in severely curved canals (Arias et al., 2018; Azim et al., 2018; Erik & Ozyurek, 2018; Yilmaz et al., 2019).

ProTaper Gold is suggested to be more suitable in narrow calcified canals than Hyflex EDM, as it has a greater torsional resistance (Kaval et al., 2016; Silva et al., 2018). It was seen to have a high content of martensitic phases but detailed information on transition temperatures is lacking and so the exact phases at intracanal temperature is unknown. WaveOne Gold may have mostly R-phases depending on intracanal temperature (Pedulla et al., 2019). The other martensitic files may have some austenitic phases like Vortex Blue, Reciproc Blue and One Curve.

XP-EndoShaper is martensitic initially on insertion into the canal and changes to austenitic between 32 - 37 °C (Adiguzel et al., 2018). The XP-EndoShaper file was found to have a greater resistance to cyclic fatigue than Hyflex EDM, in just one study using a hollow tube design (Azim et al., 2018). The XP-EndoShaper file shows that the factors which affect cyclic fatigue act in combination such as taper, swaggering movement, a small core, changes in metal phases and this file could be using the various factors in combination to increase its resistance to cyclic fatigue.

The range for intracanal temperature is wide from 30.8 - 36 °C (Cunningham et al.,1980; De Hemptinne et al., 2015; De Vasconcelos et al., 2016) which has implications for many of these files which transition within this range. Many of the tests using body temperature are testing these files at a higher temperature than needed with higher temperatures showing a reduction in cyclic fatigue resistance but these were static tests

(Alfawaz et al., 2018, De Vasconcelos et al., 2016; Dosanjh et al., 2017; Klymus et al., 2018; Plotino et al., 2018; Staffoli et al., 2018). Keles et al. (2019) used a dynamic test which showed no effect of temperature on the cyclic fatigue resistance on the reciprocating files tested.

As the XP-EndoShaper file shows a change from martensitic to austenitic in the canal, intracanal temperature and ways to lower this temperature can be significant, as at a lower temperature the file would then be operating in the martensitic phase (Grande et al., 2017); the cooler temperature having other beneficial effects such as reducing pain and inflammation (Vera et al., 2015; Vera et al., 2018). There needs to be more research into intracanal temperature and variables affecting this and transition temperatures for NiTi alloys. A detailed insight into the transition of phases and the effect this may have on cyclic fatigue resistance as there are potentially many martensitic phases and the accumulation of stresses across the martensitic structure varies (Kimiecik et al., 2013). Cyclic fatigue tests need standardisation and possibly two separate types of tests, a static test which can make it easier to compare different files and a dynamic test which can give the clinician a better comparison of how the file would work in a clinical setting.

6.1. Areas for future research:

Differential scanning calorimetry tests and cyclic fatigue tests need standardisation. Both static and dynamic cyclic fatigue testing methods have its own value; methods to incorporate both by standardisation would be useful. New research into intracanal temperature to provide a more accurate range is needed and the effect of cryotherapy could be explored. Another area for research could be exploring the effect of reciprocation on the cyclic fatigue resistance of a Hyflex EDM type file. There needs to be more research on the transition temperatures for XP-EndoShaper, ProTaper Gold and OneCurve file.

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Appendix A

Data Extraction table on Tests having outcome with Number of cycles to failure (NCF) (Author’s own work, 2019).

ID	T/°C	CC & R	Canal	SS	NiTi file	FS	Taper	Speed &Torque	Results (NCF)	
1	37°	60° 3mm No distance from tip	1.5 mm width Metal block	20	XP-endo shaper	30	0.01	800 rpm No Torque	3064	
				20	HyFlex CM	30	0.04	500 rpm No Torque	1121	
				20	FlexMaster	30	0.04	280 rpm No Torque	570	
				20	RaCe	30	0.04	600 rpm No Torque	446	
4	25°	60° 5 mm 5 mm from tip	Wider than the PTG f2 by 0.1 mm	15 15 15	ProTaper Gold	25	0.08 v	300 rpm No torque	DW 2.5%NaOCl 5.25%NaOCl	1239 761 878
	37°			15 15 15					DW 2.5%NaOCl 5.25%NaOCl	962 662 571
	60°			15 15 15					DW 2.5%NaOCl 5.25%NaOCl	419 326 306
									L/mm	NCF
5	37°	90° 3 mm 5mm,7mm or 9 mm tip from curve depending on insertion depth	Stainless steel canal 1.5 mm wide	10	HyFlex EDM	25	0.08 v	500 rpm not mentioned	15	831
				10					17	822
				10					19	539
				10	ProTaper Universal	25	0.08	300 rpm	15	114
				10					17	109
				10					19	64
				10	WaveOne Gold	25	0.07	WaveOne all program	15	659
				10					17	474
				10					19	330
				10	XP-endo Shaper	27	0.01	1000 rpm	15	923
				10					17	1031
				10					19	938
				10	XP-endo Shaper	27	0.01	3000rpm	15	1102
				10					17	1189
				10					19	1095

6	20° 37°	60 °3 mm radius and 4.5 mm from tip	Three point bending test with 3 pins and groove	20 20 20 20	ProTaper Universal Hyflex CM TRUShape Vortex Blue	25 25 25 25	0.08 0.06 0.06 0.06	300 rpm 500 rpm 300 rpm 500 rpm	20°C 37°C 20°C 37°C 20°C 37°C 20°C 37°C	199 134 2986 487 1372 201 1816 479
7	3° 22° 37° 60°	60° 5 mm radius	Metal canal 1.5 mm wide	30 30 30 30 30 30 30 30 30 30 30 30	EdgeFile Vortex Blue ESX Edge File Vortex Blue ESX EdgeFile Vortex Blue ESX EdgeFile Vortex Blue ESX	25 25 25 25 25 25 25 25 25 25 25 25	0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04 0.04	500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm 500 rpm	6185 4842 932 7243 2062 466 1675 1233 271 901 651 218	
8	37°	SC: 60° 5 mm radius 8 mm from tip. DC: 60° 5 mm radius6 mm from tip 70° 2 mm radius 2 mm from tip	Stainless steel 30/0.08	20 20 20 20 20 20 20 20 20 20	OneCurve 2Shape Vortex Blue P.Vortex RaCe OneCurve 2Shape Vortex Blue P.Vortex RaCe OneCurve 2Shape Vortex Blue P.Vortex RaCe	25 25 25 25 25 25 25 25 25 25	0.06 0.06 0.06 0.06 0.06 0.06 0.06 0.06 0.06 0.06	Manufacturer's speed and Torque In double curvature for coronal fragment included time recorded after apical fracture.	385 358 512 306 206 308 292 337 245 124 260 250 296 191 92	
9	37°	60° 3 mm radius	Three point bending test.	30 30 30 30 30	XP-endoShaper Vortex Blue HyFlex CM iRaCe TRUShape	30 30 30 30 30	0.01 0.04 0.04 0.04 0.06	Manufactures recommended speed and torque	564 465 482 146 251	
10	37°	60° 5 mm radius	Ceramic canals Custom made for size and taper	20 20 20 20 20 20 20	Reciproc B WOG HEDM Reciproc B WOG HEDM Reciproc B	25 25 25 25 25 25 25 25 25	0.08 0.07 0.08 0.08 0.07 0.08 0.08 0.07 0.08	Manufacturers recommended programmes and torque "WaveOne all"	DW 6% NaOCl 17 % EDTA	1544 1490 1712 1449 1442 1662 1469 1444 1673

				20 20 20 20 20 20 20 20	WOG HEDM Reciproc B WOG HEDM Reciproc B WOG HEDM	25 25 25 25 25 25	0.08 0.07 0.08 0.08 0.07 0.08	“Reciproc all” 500 rpm 2.5 Ncm for HEDM	18 % HEBP 6 % NaOCl +18% HEBP	1409 1367 1655 1290 1015 1412
12	35°	60 ° 5 mm radius	Metal stainless steel 1.4 mm diameter	18 18 18	XP-endo Shaper ProTaper Gold K3XF	30 30 30	0.01 0.09 v 0.04	800 rpm, 1 Ncm 300 rpm, 3 Ncm 300 rpm, 3 Ncm	3194 885 496	
13	20° 37°	60° 5 mm radius 5 mm from tip	Stainless steel custom made	10 10 10 10 10 10	Reciproc B X1 WOG Reciproc B X1 WOG	25 25 25 25 25 25	0.08 0.06 0.07 0.08 0.06 0.07	Reciproc WaveOne WaveOne Reciproc WaveOne WaveOne	3473 3726 1919 1521 1647 1533	
14	20° 35°	60°5 mm radius	Metal custom made	15 15 15 15 15 15 15 15	ProTaper Universal ProTaper Gold ProTaper Universal ProTaper Gold	S1 F2 S1 F2 S1 F2 S1 F2	0.02 0.08 0.02 0.08 0.02 0.08 0.02 0.08	300 rpm	515 228 674 504 380 114 629 457	
16	37°	60°5 mm radius	Steel custom made	25 25	OneCurve OneShape	25 25	0.06 0.06	300rpm 400rpm no torque	721 301	
17	37°	60° 5mm radius and 5 mm from tip	Custom canals 0.4 mm apical	10 10	XP-endoShaper TRUShape	30 30	0.01 0.06 v	800 rpm, 1Ncm 300 rpm, 3Ncm	1653 496	
18	0 ° 20° 35°	60° 5mm radius and 5 mm from tip	Custom made ceramic	20 20 20 20 20 20 20 20 20	OneShape OSNG OneCurve OneShape OSNG OneCurve OneShape OSNG OneCurve	25 25 25 25 25 25 25 25 25	0.06	300 rpm	1839 2628 3879 462 474 1513 298 295 657	

19	35°	60° 5mm radius and 5 mm from tip	Custom-made stainless-steel canal	20 20 20 20	WOG Reciproc B OneCurve HEDM	25 25 25 25	0.07 0.08 0.06 0.08	WaveOne Reciproc 450 rpm 500 rpm	1355 1246 864 1647	
20	37°	Single curve: 60°5 mm radius Double Curve: 60°5 mm radius 30°2 mm radius 2 mm from tip	Ceramic canals custom made to size of PTG F1 with 0.5 mm added space	13 13 13 13 13 13 13 13	ProTaper Universal ProTaper Gold ProTaper Universal ProTaper Gold	20 20 20 20 20 20 20 20	0.07 0.07 0.07 0.07 0.07 0.07 0.07 0.07	PTU: 300 rpm 250 gcm PTG: 300 rpm 150 gcm	Water NaOCl Water NaOCl Water NaOCl Water NaOCl	343 266 667 662 303 298 591 533
21	20° 37°	60° 5mm radius 5 mm from tip	Three-point bend test,19 mm insertion of file	30 30 30 30 30 30	Reciproc WOG Reciproc WOG Reciproc WOG	25 25 25 25 25 25	0.08 0.07 0.08 0.07 0.08 0.07	Reciproc ALL WaveOne ALL	Air Air Saline Saline NaOCl NaOCl	1251 1506 913 1066 880 991
22	37°	90° 2 mm radius	Stainless steel canal	18 18	Reciproc Blue Reciproc	25 25	0.08 0.08	Reciproc ALL Reciproc ALL 300rpm	1056 509	

Key
ID: Study ID, T: Temperature, CC: canal curvature, R: radius of curvature of canal, SS: Sample size, FS: file size, DW : distilled water, NaOCl : sodium hypochlorite, HEBP: etidronic acid, Rpm: rotations per minute, HEDM: Hyflex EDM, PTG: ProTaper Gold, PTU: ProTaper Universal, OSNG: OneShape New Generation file, WOG: WaveOne Gold file, Reciproc B: Reciproc Blue, P.Vortex: Profile Vortex, L: length or insertion depth of file, Ncm : Newton centimetre or torque measurement, gcm: gram centimetre or anther unit of torque. SC: single curve, DC: double curve.
S1: 18 size, F1: 20 size 0.07 taper , F2: 25 size

The Study ID created identifies the study for next two data extraction tables.

Appendix A compares studies which have measured the number of cycles to fracture as an outcome. Appendix B shows the studies which had results measured outcome as mean life or time to fracture in seconds. These were study ID 2, 3 ,11 and 15, which have been placed grouped together in Appendix B.

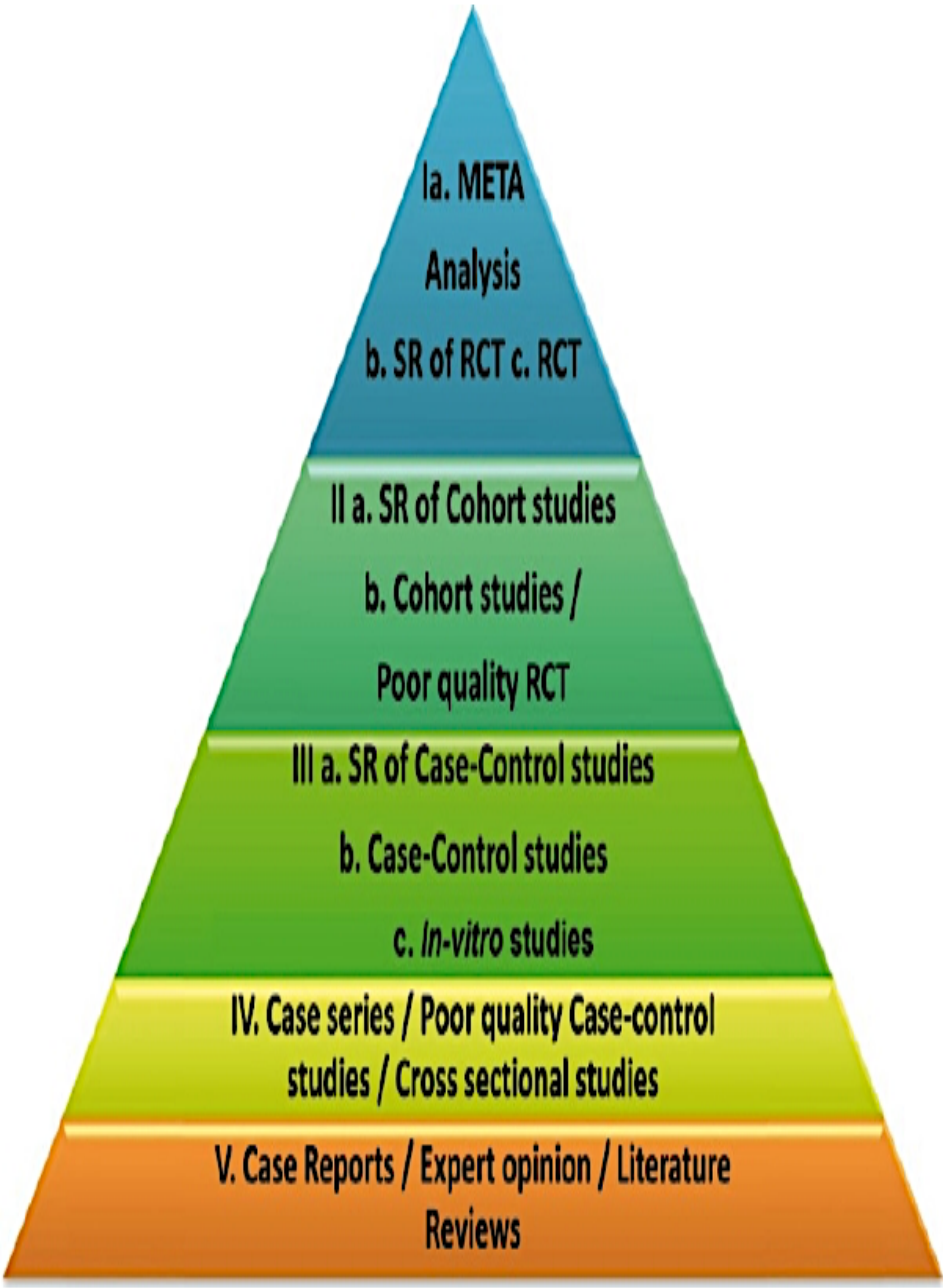
Appendix B

Tests with Mean life (ml) in seconds or Time to failure (TTF) in seconds(Author's own work, 2019).

ID	T/°C	CC / Radius	Type	SS	NiTi file	fs	Taper	Speed & torque	ml /TTF (seconds)		
2	37°	60° 3mm	Three						21°C	37°C	
	21°	4.5 mm	point	20/20	Vortex	20	0.04	500 rpm No	312	94	ml
		from tip	bendin	20/20	Blue	25	0.04	Torque	342	141	ml
			g test	20/20		30	0.04		214	98	ml
			with 3	20/20		35	0.04		147	88	ml
			pins	20/20		40	0.04		126	81	ml
			and	20/20	Edge	20	0.04	500 rpm No	253	83	ml
			groove	20/20	Sequel	25	0.04	torque	341	79	ml
				20/20	Sapphire	30	0.04		264	51	ml
				20/20		35	0.04		329	77	ml
				20/20		40	0.04		247	56	ml
3	37°	60° 3mm	Three						22°C	37°C	
	22°	5 mm from tip	point bendin	20/20	HEDM	25	0.08	400 rpm No Torque	725	718	ML
			g test	20/20	TRUShap e	25	0.06	300 rpm No torque	235	83	ML
11	22°	60° 5 mm	1.5 mm	15	WaveOne	25	0.07	Wave One	Static		106
		radius	stainles	15				All program	Dynamic		178
			s steel	15	WaveOne	25	0.07	for Wave	Static		175
				15	Gold			One	Dynamic		259
				15	Reciproc	25	0.08	Reciproc all	Static		197
				15				program for	Dynamic		292
				15	Reciproc	25	0.08	Reciproc	Static		214
				15	Blue			files. Both	Dynamic		276
	35°			15	WaveOne	25	0.07	reciprocatin	Static		102
				15				g	Dynamic		107
				15	WaveOne	25	0.07	movements	Static		150
				15	Gold				Dynamic		221
				15	Reciproc	25	0.08		Static		225
				15					Dynamic		273
				15	Reciproc	25	0.08		Static		254
				15	Blue				Dynamic		253
15	0°	60 ° 5 mm	Stainle	20	Reciproc	25	0.08	Reciproc All	400		ML in
		radius and	ss steel	20	Reciproc	25	at tip		544		seconds
	20°	6 mm from		20	Blue	25	and		150		ML in
		tip		20	Reciproc	25	0.04		395		seconds
	35°			20	Reciproc	25	at		106		ML in
				20	Blue	25	shaft		191		seconds
	39°			20	Reciproc	25			77		ML in
				20	Reciproc	25			141		seconds
					Blue						
					Reciproc						
					Reciproc						
					Blue						
ID: Study ID, T : Temperature, CC: Canal Curvature, fs: file size, SS: Sample size.											

Appendix C

Levels of evidence. From " Research methodology in Dentistry: Part I – The essentials and relevance of research," by J., Krithikadatta, 2012, *Journal of Conservative Dentistry,* 15(1), 5–11.



Appendix D

Percentage of Nickel and titanium in Hyflex EDM compared to Hyflex CM. From "Structural analysis of HyFlex EDM instruments," by Iacono et al., 2017, *International Endodontic Journal*, *50*(3), p.308.

Table 3 Semi-quantitative EDS chemical analysis of the surface layer in studied instruments (average ± SD)

	HyFlex CM	HyFlex EDM
Ni (at.%)	13.3 ± 1.5	27.5 ± 7.9
Ti (at.%)	35.1 ± 0.7	45.6 ± 1.3
O (at.%)	48.4 ± 1.8	22.6 ± 8.4
S (at.%)	0.4 ± 0.1	–
C (at.%)	2.9 ± 0.3	4.3 ± 0.7

Appendix E

Risk of bias assessment. From "Assessing risk of bias in included studies" Cochrane Handbook, by Higgins and Green, 2011, (https://handbook-5-1.cochrane.org/chapter_8/table_8_4_a_a_common_classification_scheme_for_bias.htm).

Type of bias	**Description**	**Relevant domains in the Collaboration's 'Risk of bias' tool**
Selection bias	Systematic differences between baseline characteristic of the groups that are compared	Sequence generation Allocation concealment
Performance bias	Systematic differences between groups in the care that is provided or in exposure to factors other than interventions of interest.	Blinding of participants and personnel Other potential threats to validity
Detection bias	Systematic differences between groups in how outcomes are determined	Binding of outcome assessment Other potential threats to validity
Attrition bias	Systematic differences between groups in withdrawals from the study	Incomplete outcome data
Reporting bias	Systematic differences between reported and unreported findings	Selective outcome reporting.

Appendix F

27-point checklist. From "The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration," by Liberati et al., 2009, *Journal of Clinical Epidemiology*, *62*(10),p. e4.

Section/Topic	#	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

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